STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 94890

TO: Molly Ceperley Location:cm1 7E12 Art Unit: 1614 Thursday, May 29, 2003 Cas Serial Number: 820210	From: Alex Waclawiw Location: Biotech-Chem Library CM1-6A02 Phone: 308-4491 Alexandra.waclawiw@uspto.gov

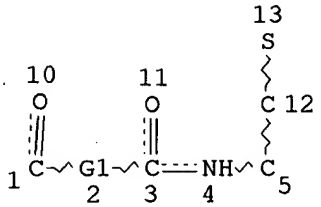
Search Notes

09/820,210

```
=> d his

     (FILE 'HCAPLUS' ENTERED AT 09:45:17 ON 29 MAY 2003)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 09:45:31 ON 29 MAY 2003
               ACT CEPERLY2/A
              ---------
L1             STR
L2             SCR 1199 AND 2021
L3             STR
L4   (       452)SEA FILE=REGISTRY SSS FUL L3 AND L2
L5            30 SEA FILE=REGISTRY SUB=L4 SSS FUL L1
              ---------
L6            28 S L5 AND (CAPLUS OR CA)/LC
L7             5 S L5 AND USPATFULL/LC
L8             0 S L7 NOT L6

     FILE 'HCAPLUS' ENTERED AT 09:46:15 ON 29 MAY 2003
L9            14 S L5

     FILE 'HCAPLUS' ENTERED AT 09:46:18 ON 29 MAY 2003

     FILE 'HCAOLD' ENTERED AT 09:46:31 ON 29 MAY 2003
L10            0 S L5
```

Considered
05/30/03
MEC

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 09:46:39 ON 29 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   28 MAY 2003  HIGHEST RN 521913-14-4
DICTIONARY FILE UPDATES:  28 MAY 2003  HIGHEST RN 521913-14-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d que stat l5
L1                STR

                 13
                  S
 10      11       
  O       O      C 12
                    6
1 C-G1-C-NH-C-C-NH-Ak-NH
    2  3  4  5  7  8  9
                  O
                 14


REP G1=(2-5) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  14

STEREO ATTRIBUTES: NONE
L2                SCR 1199 AND 2021
L3                STR
```



REP G1=(2-5) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L4 (452)SEA FILE=REGISTRY SSS FUL L3 AND L2
L5 30 SEA FILE=REGISTRY SUB=L4 SSS FUL L1

100.0% PROCESSED 107 ITERATIONS 30 ANSWERS
SEARCH TIME: 00.00.01

=> d his 16-18

(FILE 'REGISTRY' ENTERED AT 09:45:31 ON 29 MAY 2003)

L6 28 S L5 AND (CAPLUS OR CA)/LC
L7 5 S L5 AND USPATFULL/LC
L8 0 S L7 NOT L6

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:46:55 ON 29 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 29 May 2003 VOL 138 ISS 22
FILE LAST UPDATED: 28 May 2003 (20030528/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos 19
L1 STR
L2 SCR 1199 AND 2021
L3 STR
L4 (452) SEA FILE=REGISTRY SSS FUL L3 AND L2
L5 30 SEA FILE=REGISTRY SUB=L4 SSS FUL L1
L9 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L5

=> d .ca hitstr 19 1-14

L9 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946261 HCAPLUS
DOCUMENT NUMBER: 138:14180
TITLE: Preparation of peptide-related hydroxyalkylamines for pharmaceutical use in the treatment of Alzheimer's disease
INVENTOR(S): Freskos, John; Aquino, Jose; Brown, David L.; Fang, Larry; Fobian, Yvette M.; Gailunas, Andrea; Guinn, Ashley; Varghese, John; Romero, Arthur Glenn; Tucker, John; Tung, Jay; Walker, Donald
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098849	A2	20021212	WO 2002-US17698	20020531

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-295332P P 20010601
US 2001-332639P P 20011119
US 2001-343772P P 20011228

OTHER SOURCE(S): MARPAT 138:14180
AB Hydroxyalkylamines RNNR20CHR1CH(OH)CR2R3NR20Rc [RN is an acyl group of defined structure; R20 is H, (un)substituted alkyl, alkoxy, alkoxy-, hydroxy-, or haloalkyl, or -R26-R27, where R26 is CO, SO2, CO2, CONH, or alkylcarbamoyl and R27 is (un)substituted alkyl, alkoxy, arylalkyl, heterocycloalkyl, or heteroaryl; R1 is -(CH2)1-2-S(O)0-2-alkyl, (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl, heterocyclyl, etc.; R2, R3 are H or (un)substituted alkyl or CR2R3 is a 3-7 membered carbocycle in which one carbon atom is optionally replaced by O, S, SO2,

or NRN-2; Rc is (un)substituted alkyl, (hetero)arylalkyl, heterocyclylalkyl, etc.] were prepd. for treating Alzheimer's disease and similar diseases. Synthetic procedures are given in examples and schemes. Several hundred products of the invention are listed in a table and in the claims, including S-butyl-N-1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl]-D-cysteinamide.

IC ICM C07C317-26
ICS C07C323-39; C07C271-18; C07D309-10; C07D207-26; A61K031-33; A61K031-325; A61K031-165; C07D211-16

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63

IT 388064-69-5P 477790-42-4P 477790-46-8P 477790-49-1P 477790-56-0P
477790-62-8P 477790-63-9P 477790-64-0P 477790-65-1P 477790-66-2P
477790-67-3P 477790-68-4P 477790-69-5P 477790-70-8P 477790-71-9P
477790-72-0P 477790-73-1P 477790-74-2P 477790-75-3P 477790-76-4P
477790-77-5P 477790-78-6P 477790-79-7P 477790-80-0P 477790-81-1P
477790-82-2P 477790-83-3P 477790-84-4P 477790-85-5P 477790-86-6P
477790-87-7P 477790-88-8P 477790-89-9P 477790-90-2P 477790-91-3P
477790-92-4P 477790-93-5P 477790-94-6P 477790-96-8P 477790-98-0P
477790-99-1P 477791-00-7P 477791-01-8P 477791-02-9P 477791-03-0P
477791-04-1P 477791-05-2P 477791-06-3P 477791-07-4P 477791-08-5P
477791-09-6P 477791-10-9P 477791-11-0P 477791-12-1P 477791-13-2P
477791-14-3P 477791-15-4P 477791-16-5P 477791-17-6P 477791-18-7P
477791-19-8P 477791-20-1P 477791-21-2P 477791-22-3P 477791-23-4P
477791-24-5P 477791-25-6P 477791-26-7P 477791-27-8P 477791-28-9P
477791-29-0P 477791-30-3P 477791-31-4P 477791-32-5P 477791-33-6P
477791-34-7P 477791-35-8P 477791-36-9P 477791-37-0P 477791-38-1P
477791-39-2P 477791-40-5P 477791-41-6P 477791-42-7P 477791-43-8P
477791-44-9P 477791-45-0P 477791-46-1P 477791-47-2P 477791-48-3P
477791-49-4P 477791-50-7P 477791-51-8P 477791-52-9P 477791-53-0P
477791-54-1P 477791-55-2P 477791-56-3P 477791-57-4P 477791-58-5P
477791-59-6P 477791-60-9P 477791-61-0P 477791-62-1P 477791-63-2P
477791-64-3P 477791-65-4P 477791-66-5P 477791-67-6P 477791-68-7P
477791-69-8P 477791-70-1P 477791-71-2P 477791-72-3P 477791-73-4P
477791-74-5P 477791-75-6P 477791-76-7P 477791-77-8P 477791-78-9P
477791-79-0P 477791-80-3P 477791-81-4P 477791-82-5P 477791-83-6P
477791-84-7P 477791-85-8P 477791-86-9P 477791-87-0P 477791-88-1P
477791-89-2P 477791-90-5P 477791-91-6P 477791-92-7P 477791-93-8P
477791-94-9P 477791-95-0P 477791-96-1P 477791-97-2P 477791-98-3P
477791-99-4P 477792-00-0P 477792-01-1P 477792-02-2P 477792-03-3P
477792-04-4P 477792-05-5P 477792-06-6P 477792-07-7P 477792-08-8P
477792-09-9P 477792-10-2P 477792-11-3P 477792-12-4P 477792-13-5P
477792-14-6P 477792-15-7P 477792-16-8P 477792-17-9P 477792-18-0P
477792-19-1P 477792-20-4P 477792-21-5P 477792-22-6P 477792-24-8P
477792-25-9P 477792-26-0P 477792-28-2P 477792-29-3P 477792-30-6P
477792-31-7P 477792-32-8P 477792-33-9P 477792-34-0P 477792-35-1P
477792-36-2P 477792-37-3P 477792-38-4P 477792-39-5P 477792-40-8P
477792-41-9P 477792-42-0P 477792-43-1P 477792-44-2P 477792-45-3P
477792-46-4P 477792-47-5P 477792-48-6P 477792-49-7P 477792-50-0P
477792-51-1P 477792-52-2P 477792-53-3P 477792-54-4P 477792-55-5P
477792-56-6P **477792-57-7P** **477792-58-8P**
477792-59-9P 477792-60-2P 477792-61-3P 477792-62-4P
477792-63-5P 477792-64-6P 477792-65-7P 477792-66-8P 477792-67-9P
477792-68-0P 477792-69-1P 477792-70-4P 477792-71-5P 477792-72-6P
477792-73-7P 477792-74-8P 477792-75-9P 477792-76-0P 477792-77-1P
477792-78-2P 477792-79-3P 477792-80-6P 477792-81-7P 477792-82-8P
477792-83-9P 477792-85-1P 477792-87-3P 477792-88-4P 477792-89-5P
477792-90-8P 477792-91-9P 477792-92-0P 477792-93-1P 477792-94-2P

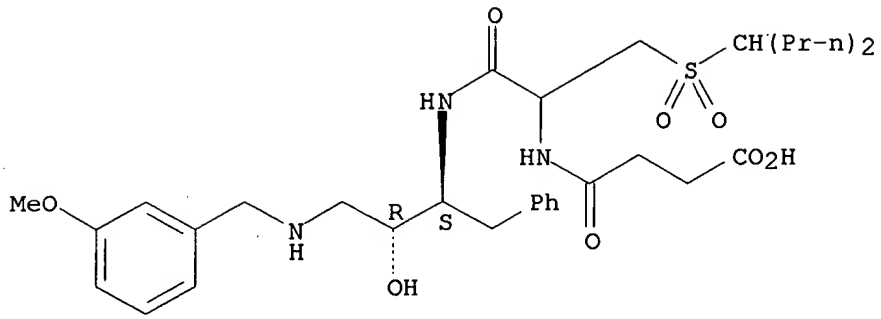
477792-95-3P 477792-96-4P 477792-97-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide-related hydroxyalkylamines for treatment of Alzheimer's disease)

IT 477792-98-6P 477792-99-7P 477793-00-3P 477793-01-4P 477793-02-5P
477793-03-6P 477793-04-7P 477793-05-8P 477793-06-9P 477793-07-0P
477793-09-2P 477793-10-5P 477793-11-6P 477793-12-7P 477793-13-8P
477793-14-9P 477793-15-0P 477793-16-1P 477793-17-2P 477793-18-3P
477793-19-4P 477793-20-7P 477793-21-8P 477793-23-0P 477793-24-1P
477793-25-2P 477793-26-3P 477793-27-4P 477793-28-5P 477793-29-6P
477793-30-9P 477793-31-0P 477793-32-1P 477793-33-2P 477793-34-3P
477793-35-4P 477793-36-5P 477793-37-6P 477793-38-7P 477793-39-8P
477793-40-1P 477793-41-2P 477793-42-3P 477793-43-4P 477793-44-5P
477793-45-6P 477793-46-7P 477793-47-8P 477793-48-9P 477793-49-0P
477793-50-3P 477793-51-4P 477793-52-5P 477793-53-6P 477793-54-7P
477793-55-8P 477793-56-9P 477793-57-0P 477793-58-1P 477793-59-2P
477793-60-5P 477793-61-6P 477793-62-7P 477793-63-8P 477793-64-9P
477793-65-0P 477793-66-1P 477793-67-2P 477793-68-3P 477793-69-4P
477793-70-7P 477793-71-8P 477793-72-9P 477793-73-0P 477793-74-1P
477793-75-2P 477793-76-3P 477793-77-4P 477793-78-5P 477793-79-6P
477793-80-9P 477793-81-0P 477793-82-1P 477793-83-2P 477793-84-3P
477793-85-4P 477793-86-5P 477793-87-6P 477793-88-7P 477793-89-8P
477793-90-1P 477793-91-2P 477793-92-3P 477793-93-4P 477793-94-5P
477793-95-6P 477793-96-7P 477793-97-8P 477793-98-9P 477793-99-0P
477794-00-6P 477794-01-7P 477794-02-8P 477794-03-9P 477794-04-0P
477794-05-1P 477794-06-2P 477794-07-3P 477794-08-4P 477794-09-5P
477794-10-8P 477794-11-9P 477794-12-0P 477794-13-1P 477794-14-2P
477794-15-3P 477794-16-4P 477794-17-5P 477794-18-6P 477794-19-7P
477794-20-0P 477794-21-1P 477794-22-2P 477794-23-3P 477794-24-4P
477794-25-5P 477794-26-6P 477794-27-7P 477794-28-8P 477794-29-9P
477794-30-2P 477794-31-3P 477794-32-4P 477794-33-5P 477794-34-6P
477794-35-7P 477794-36-8P 477794-37-9P 477794-38-0P 477794-39-1P
477794-40-4P 477794-41-5P 477794-42-6P 477794-43-7P 477794-44-8P
477794-45-9P 477794-46-0P 477794-47-1P 477794-48-2P 477794-49-3P
477794-50-6P **477794-51-7P** **477794-52-8P**
477794-53-9P 477794-54-0P 477794-55-1P 477794-56-2P
477794-57-3P 477794-58-4P 477794-59-5P 477794-60-8P 477794-61-9P
477795-38-3P 477795-39-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide-related hydroxyalkylamines for treatment of Alzheimer's disease)

IT **477792-57-7P** **477792-58-8P** **477792-59-9P**
477794-51-7P **477794-52-8P** **477794-53-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide-related hydroxyalkylamines for treatment of Alzheimer's disease)

RN 477792-57-7 HCAPLUS
CN Butanoic acid, 4-[[2-[[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]amino]-2-oxo-1-[[(1-propylbutyl)sulfonyl]methyl]ethyl]amino]-4-oxo-, monohydrochloride (9CI) (CA INDEX NAME)

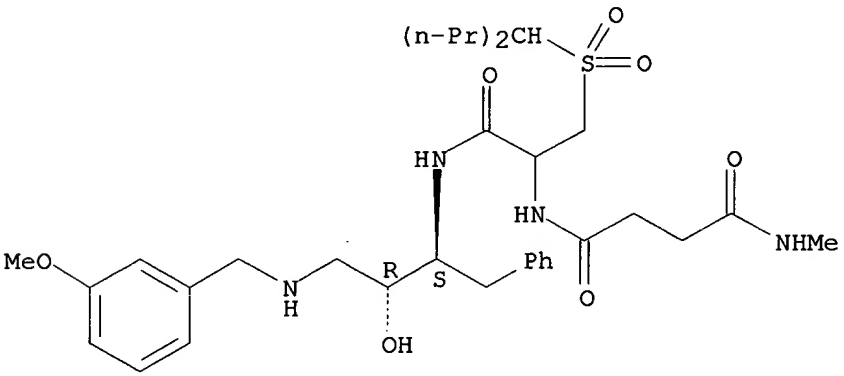
Absolute stereochemistry.



● HCl

RN 477792-58-8 HCAPLUS
CN Butanediamide, N-[2-[[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]amino]-2-oxo-1-[[(1-propylbutyl)sulfonyl]methyl]ethyl]-N'-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

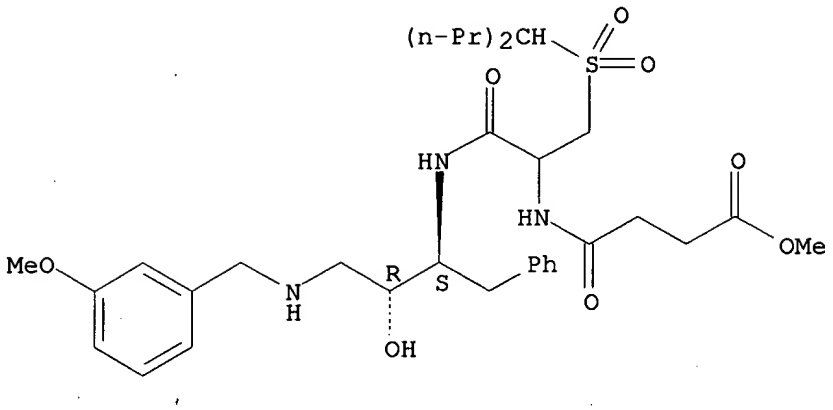
Absolute stereochemistry.



● HCl

RN 477792-59-9 HCAPLUS
CN Butanoic acid, 4-[[2-[[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]amino]-2-oxo-1-[[(1-propylbutyl)sulfonyl]methyl]ethyl]amino]-4-oxo-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

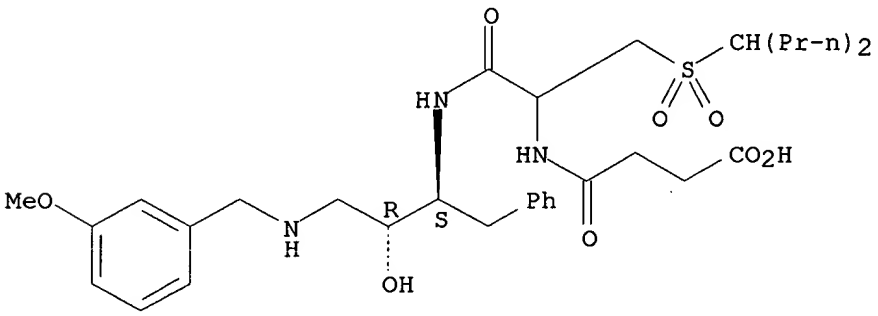
Absolute stereochemistry.



● HCl

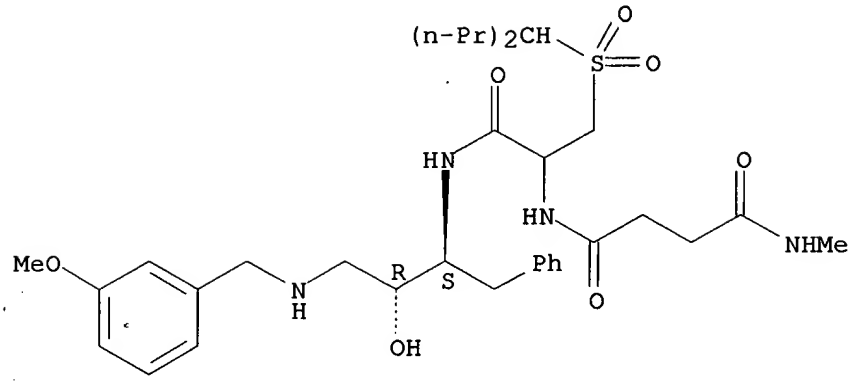
RN 477794-51-7 HCAPLUS
CN Butanoic acid, 4-[[2-[[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]amino]-2-oxo-1-[[(1-propylbutyl)sulfonyl]methyl]ethyl]amino]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



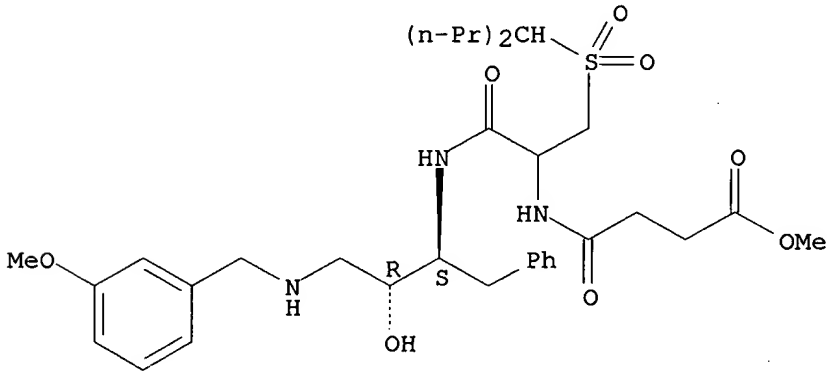
RN 477794-52-8 HCAPLUS
CN Butanediamide, N-[2-[[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]amino]-2-oxo-1-[[(1-propylbutyl)sulfonyl]methyl]ethyl]-N'-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477794-53-9 HCAPLUS
CN Butanoic acid, 4-[[2-[[(1S,2R)-2-hydroxy-3-[[(3-methoxyphenyl)methyl]amino]-1-(phenylmethyl)propyl]amino]-2-oxo-1-[[(1-propylbutyl)sulfonyl]methyl]ethyl]amino]-4-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:695821 HCAPLUS
DOCUMENT NUMBER: 137:237702
TITLE: Improved peptide-chelate conjugates
INVENTOR(S): Cuthbertson, Alan; Mendizabal, Marivi; Dixon, Mark; Storey, Anthony Eamon
PATENT ASSIGNEE(S): Amersham PLC, UK
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070018	A2	20020912	WO 2002-GB857	20020301
WO 2002070018	A3	20021205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-5224 A 20010302
OTHER SOURCE(S): MARPAT 137:237702

AB A peptide-chelate conjugate with affinity for the ST receptor is disclosed, wherein the chelate is tetradentate. The peptide-chelate conjugate of the invention may be labeled with a radiometal to provide a metal complex. A radiopharmaceutical compn. comprising the metal complex is provided, which is suitable for the diagnostic imaging of colorectal cancer. Also provided for in the invention is a kit for the prepn. of the radiopharmaceutical prepn.

IC ICM A61K047-48
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8, 34

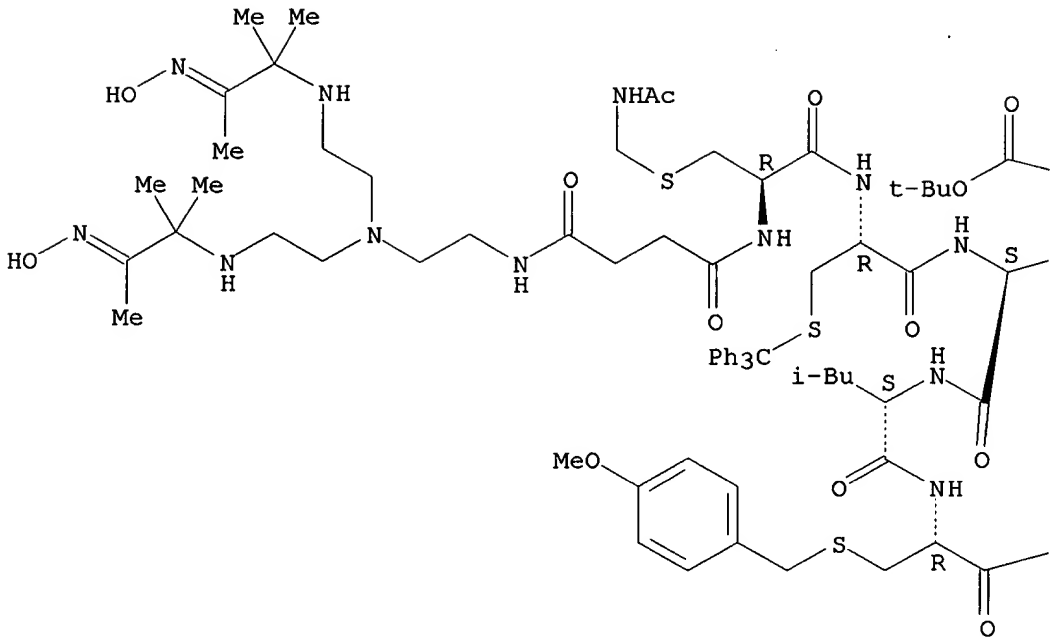
IT **457887-79-5DP**, resin-bound **457887-80-8P** 457887-81-9P 457887-82-0P 457887-83-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiolabeled peptide-chelate conjugates with affinity for ST receptor for colorectal cancer imaging)

IT **457887-79-5DP**, resin-bound **457887-80-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiolabeled peptide-chelate conjugates with affinity for ST receptor for colorectal cancer imaging)

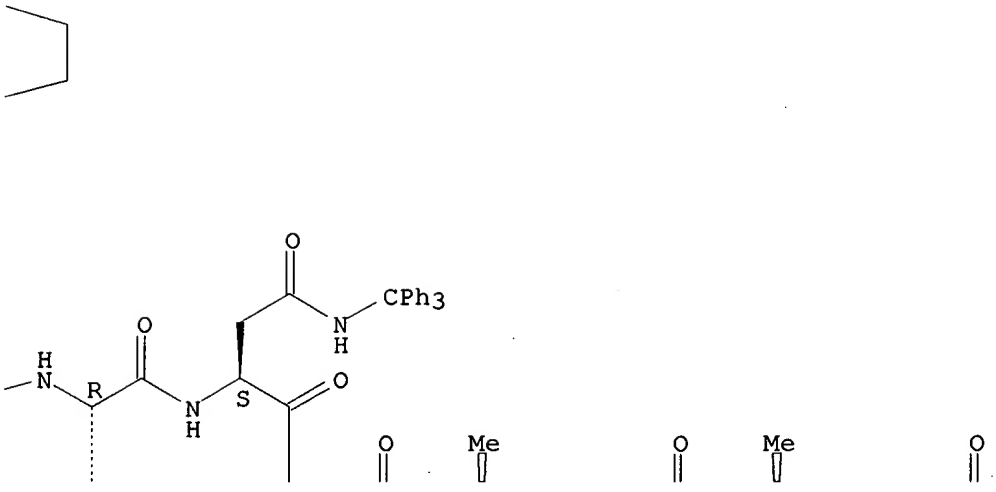
RN 457887-79-5 HCAPLUS
CN L-Tyrosine, S-[(acetylamino)methyl]-N-[4-[[2-[bis[2-[[2-(hydroxyimino)-1,1-dimethylpropyl]amino]ethyl]amino]ethyl]amino]-1,4-dioxobutyl]-L-cysteinyl-S-(triphenylmethyl)-L-cysteinyl-L-.alpha.-glutamyl-L-leucyl-S-[(4-methoxyphenyl)methyl]-L-cysteinyl-S-[(acetylamino)methyl]-L-cysteinyl-N-(triphenylmethyl)-L-asparaginyl-L-prolyl-L-alanyl-S-(triphenylmethyl)-L-cysteinyl-L-alanylglycyl-S-[(4-methoxyphenyl)methyl]-L-cysteinyl-O-(1,1-dimethylethyl)-, 3-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

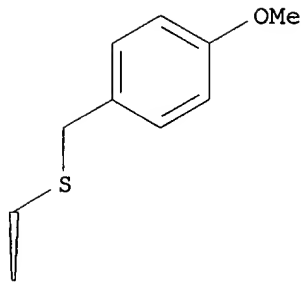
PAGE 1-A



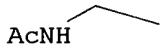
PAGE 1-B



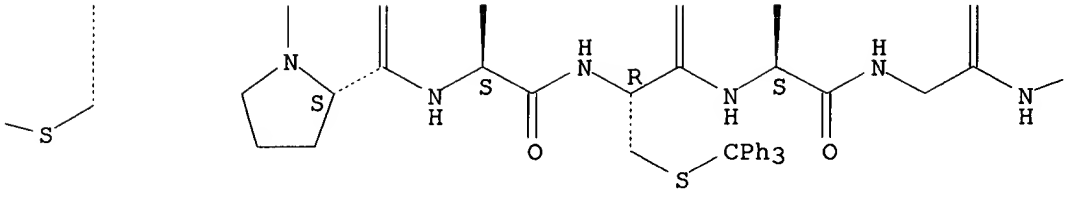
PAGE 1-C



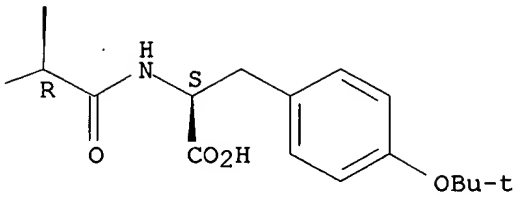
PAGE 2-A



PAGE 2-B



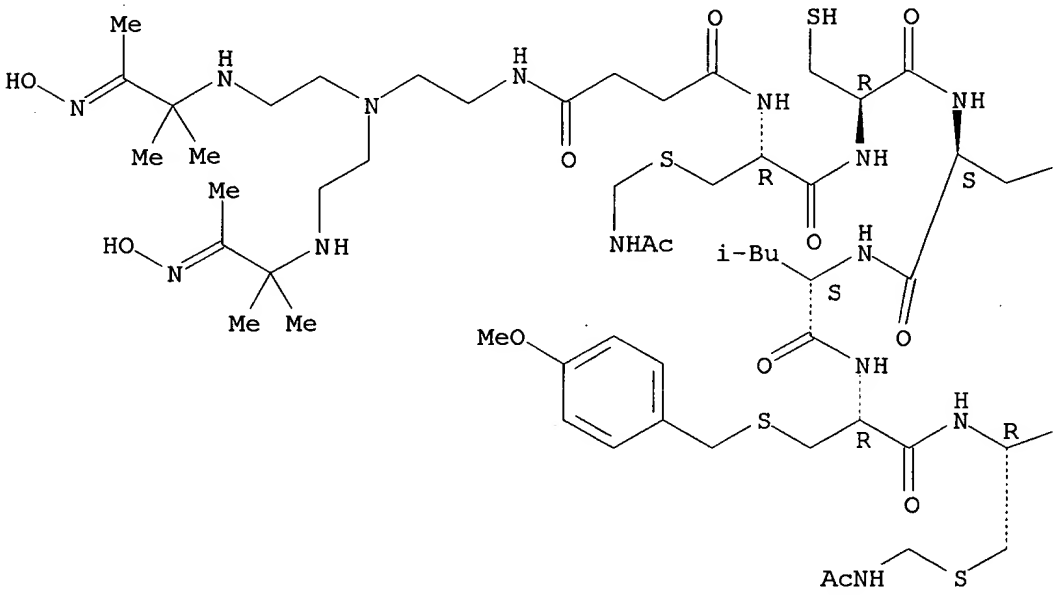
PAGE 2-C



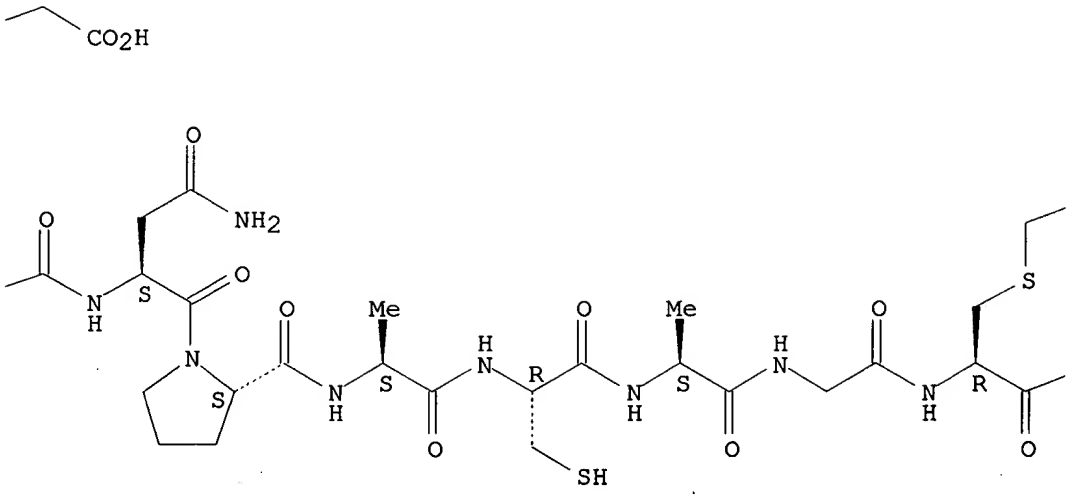
RN 457887-80-8 HCAPLUS
CN L-Tyrosine, S-[(acetylamino)methyl]-N-[4-[[2-[bis[2-[[2-(hydroxyimino)-1,1-dimethylpropyl]amino]ethyl]amino]ethyl]amino]-1,4-dioxobutyl]-L-cysteinyl-L-cysteinyl-L-.alpha.-glutamyl-L-leucyl-S-[(4-methoxyphenyl)methyl]-L-cysteinyl-S-[(acetylamino)methyl]-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-alanylglycyl-S-[(4-methoxyphenyl)methyl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

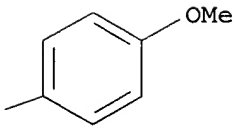
PAGE 1-A

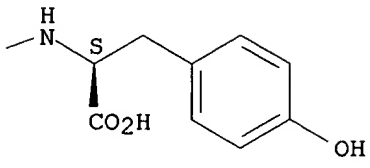


PAGE 1-B



PAGE 1-C





L9 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:332061 HCAPLUS
DOCUMENT NUMBER: 136:363880
TITLE: Synthetic regulatory compounds
INVENTOR(S): Dervan, Peter; Mapp, Anna; Ptashne, Mark; Ansari, Aseem
PATENT ASSIGNEE(S): Memorial Sloan-Kettering Cancer Center, USA; California Institute of Technology
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034295	A1	20020502	WO 2000-US29617	20001027
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001013481	A5	20020506	AU 2001-13481	20001027

PRIORITY APPLN. INFO.: WO 2000-US29617 A 20001027

AB This invention provides novel synthetic regulatory compds. that comprise a nucleic acid binding moiety, a linker, and a regulatory moiety, compns. comprising such compds., methods of designing and synthesizing such compds., methods of screening such compds. to identify those having the desired regulatory activity, and methods of using such compds. to prevent or treat disease in plants and animals, including humans. These compds., and compns. contg. them, have multiple applications, including use in human and animal medicine and in agriculture.

IC ICM A61K047-48
ICS A61K049-00

CC 1-12 (Pharmacology)
Section cross-reference(s): 3, 5, 28, 34

IT **401901-37-9P 401901-38-0P** 422551-21-1P 422551-23-3P 422551-25-5P 422551-26-6P 422551-27-7P 422551-29-9P
RL: AGR (Agricultural use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic regulatory compds. comprising nucleic acid binding moiety and linker and regulatory moiety for treatment of disease in animals and plants)

IT **401901-40-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthetic regulatory compds. comprising nucleic acid binding moiety and linker and regulatory moiety for treatment of disease in animals and plants)

IT 3194-60-3, Thiolane-2,5-dione 288573-46-6 401901-36-8 **401901-39-1** 420131-15-3 420131-16-4 420131-17-5 420270-13-9 420270-18-4 420270-19-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthetic regulatory compds. comprising nucleic acid binding moiety

and linker and regulatory moiety for treatment of disease in animals and plants)

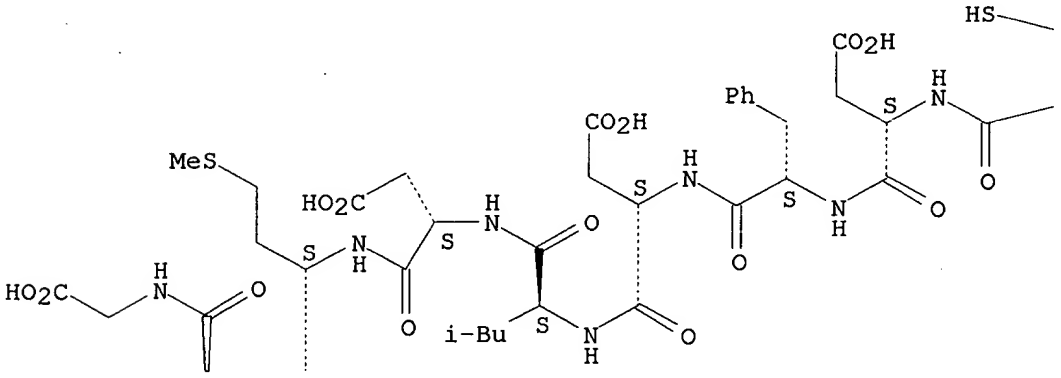
IT **401901-37-9P 401901-38-0P**
RL: AGR (Agricultural use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic regulatory compds. comprising nucleic acid binding moiety and linker and regulatory moiety for treatment of disease in animals and plants)

RN 401901-37-9 HCAPLUS

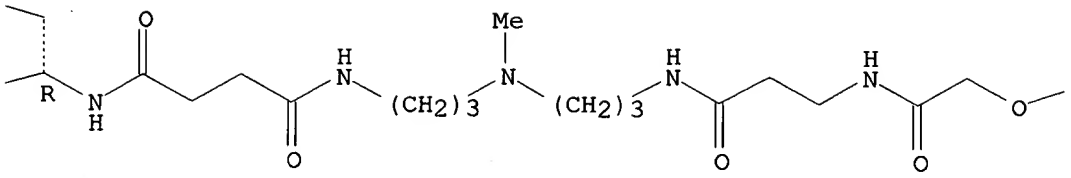
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-.beta.-alanyl-19-amino-5-oxo-3,10,13,16-tetraoxa-6-azanonadecanoyl-.beta.-alanyl-4-[[3-[(3-aminopropyl)methylamino]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

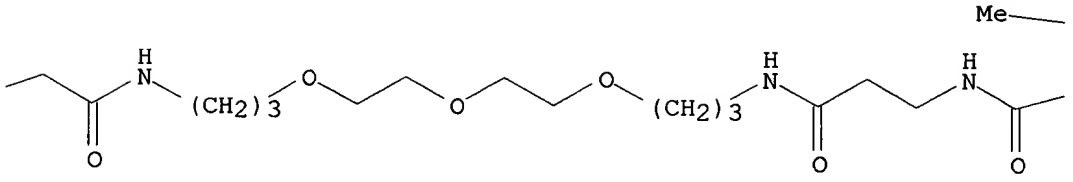
PAGE 1-A



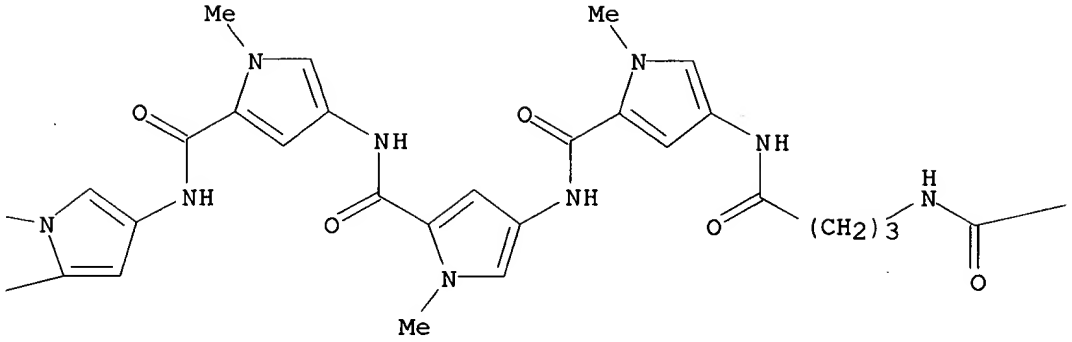
PAGE 1-B



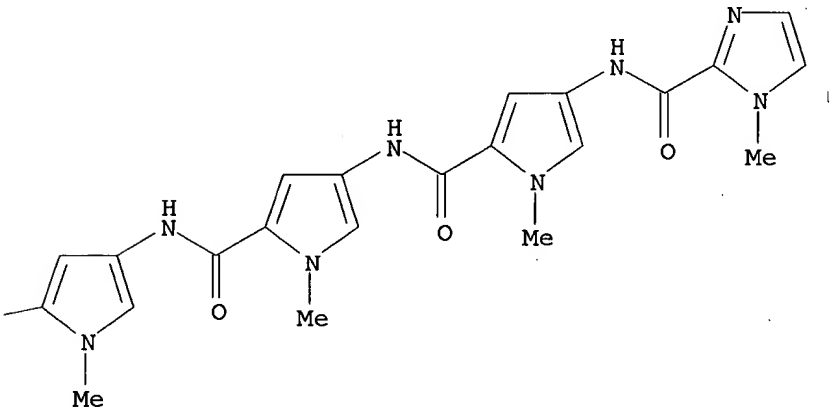
PAGE 1-C



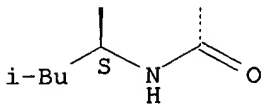
PAGE 1-D



PAGE 1-E



PAGE 2-A

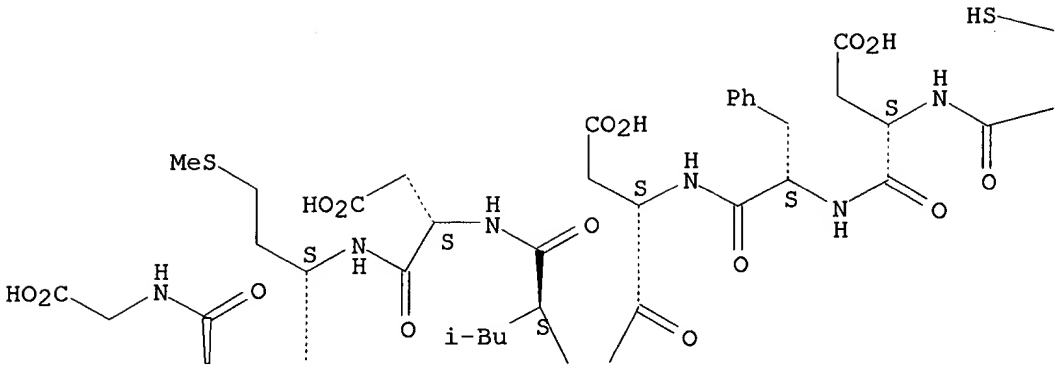


RN 401901-38-0 HCAPLUS

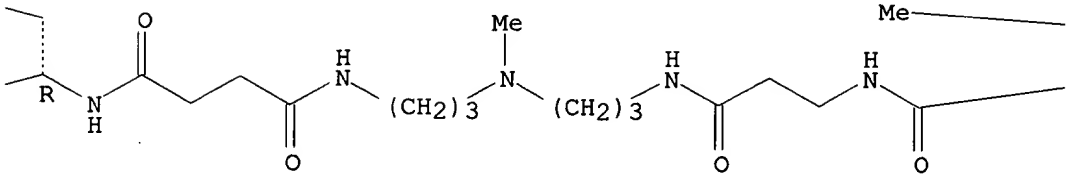
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-.beta.-alanyl-4-[[3-[(3-aminopropyl)methylamino]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

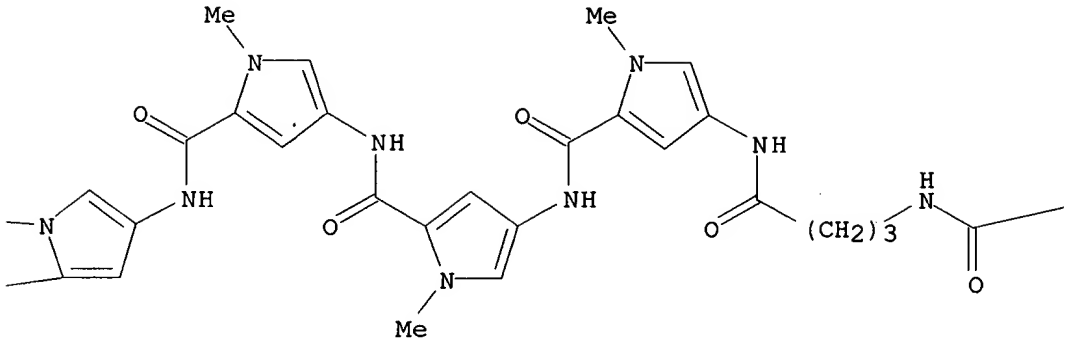
PAGE 1-A



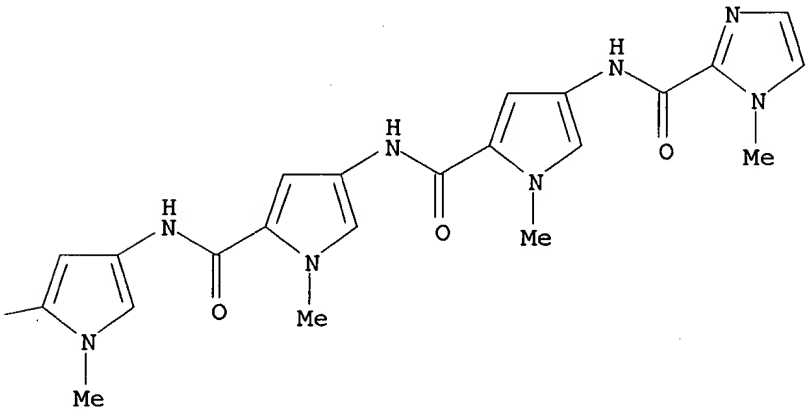
PAGE 1-B



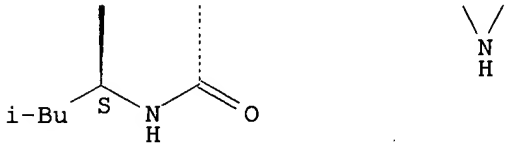
PAGE 1-C



PAGE 1-D



PAGE 2-A

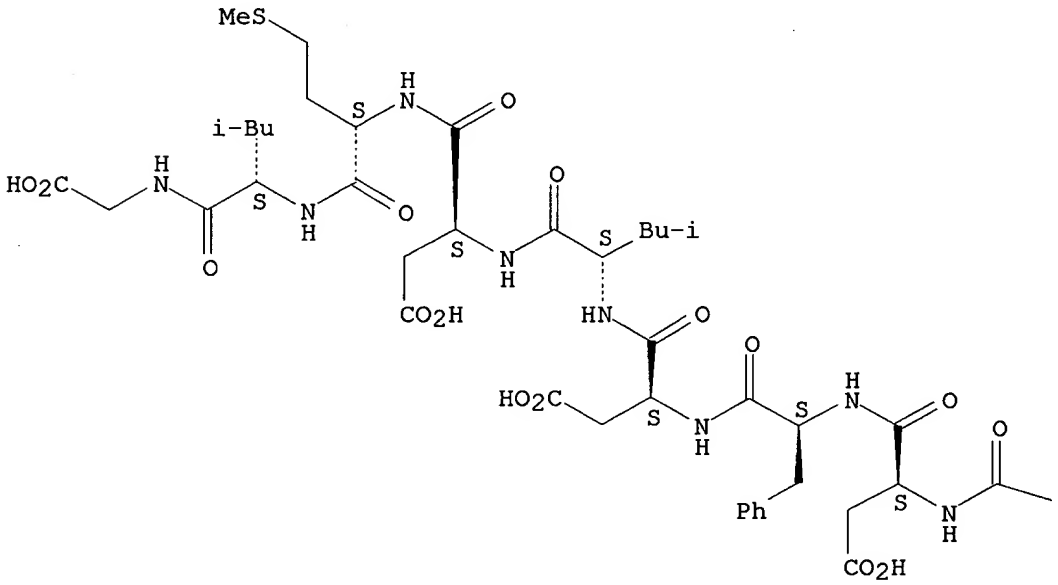


IT **401901-40-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthetic regulatory compds. comprising nucleic acid binding moiety and linker and regulatory moiety for treatment of disease in animals and plants)
RN 401901-40-4 HCAPLUS
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-

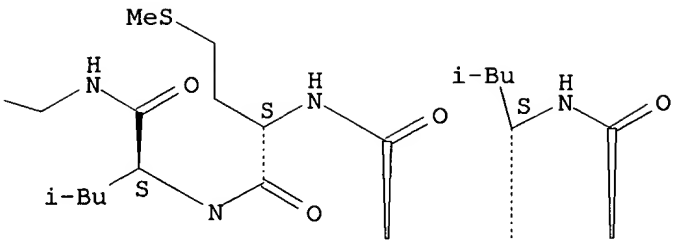
pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-[[3-[4-amino-2-[[[3-[[3-(dimethylamino)propyl]amino]-3-oxopropyl]amino]carbonyl]-1H-pyrrol-1-yl]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



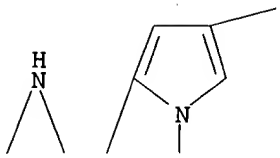
PAGE 1-B



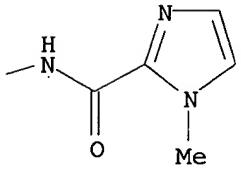
PAGE 1-C

Me

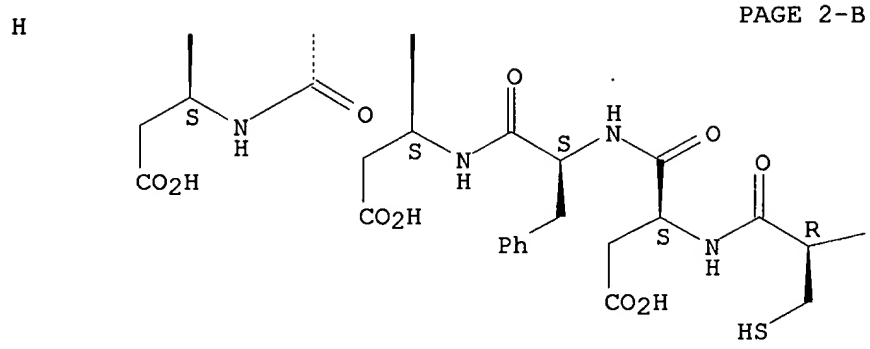
PAGE 1-D



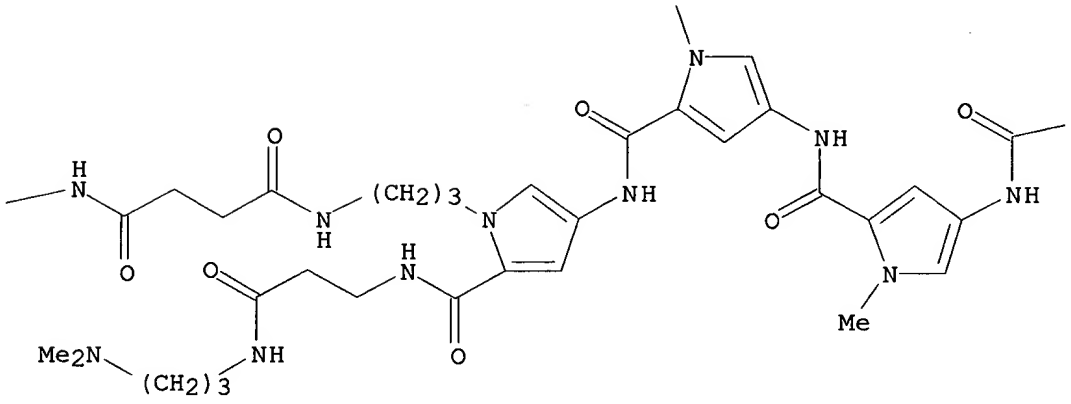
PAGE 1-E



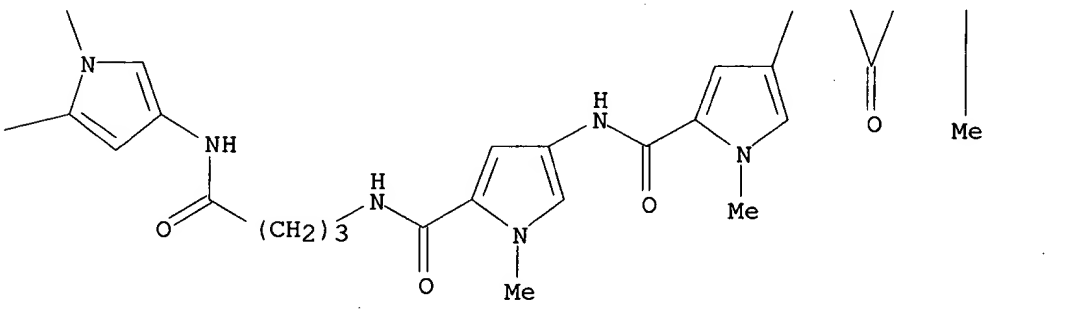
PAGE 2-B



PAGE 2-C



PAGE 2-D



IT **401901-39-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthetic regulatory compds. comprising nucleic acid binding moiety and linker and regulatory moiety for treatment of disease in animals and plants)

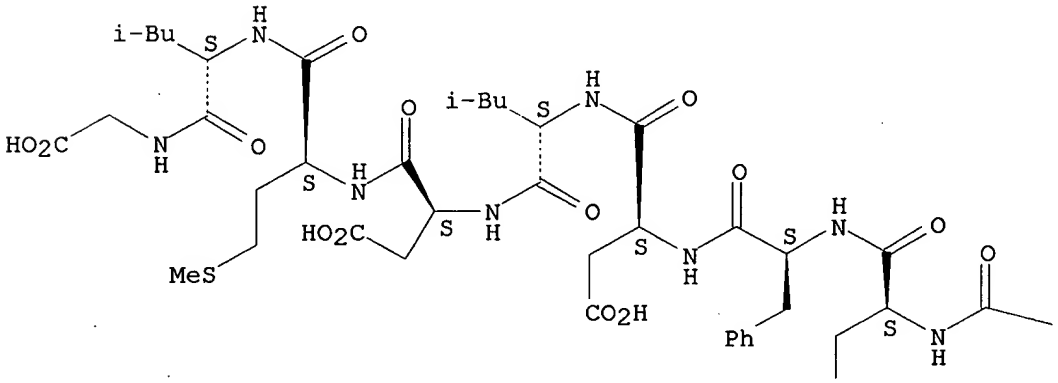
RN 401901-39-1 HCAPLUS

CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-

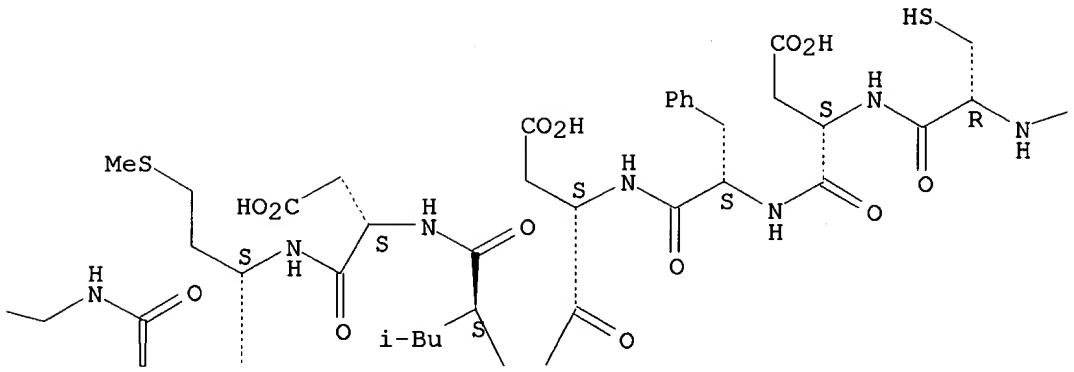
pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-.beta.-alanyl-4-[[3-[(3-aminopropyl)methylamino]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

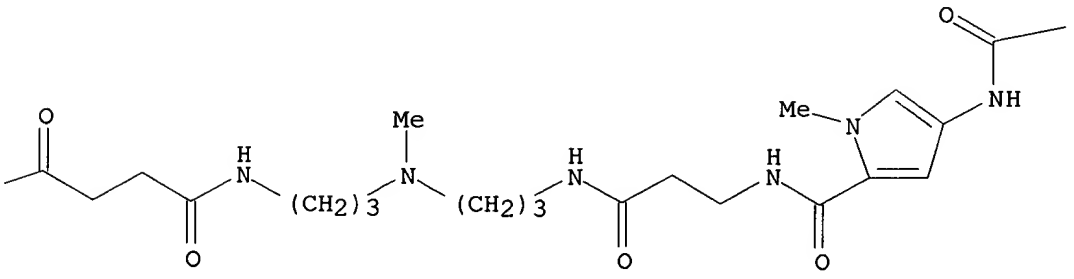
PAGE 1-A



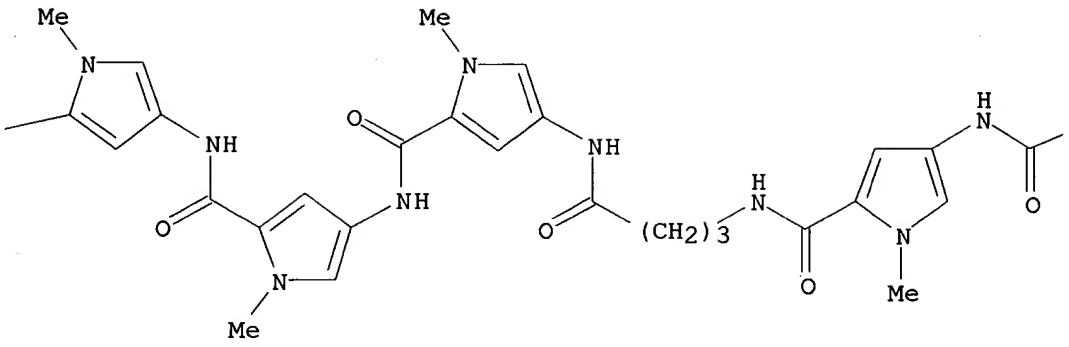
PAGE 1-B



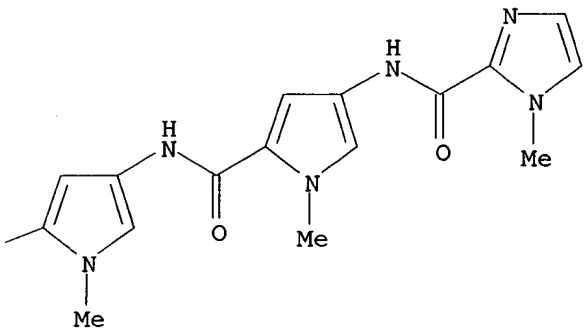
PAGE 1-C



PAGE 1-D

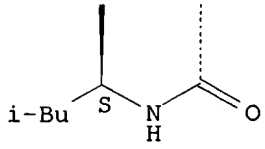


PAGE 1-E



PAGE 2-A

PAGE 2-B



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:590256 HCAPLUS
DOCUMENT NUMBER: 136:211714
TITLE: Towards a minimal motif for artificial transcriptional activators
AUTHOR(S): Ansari, Aseem Z.; Mapp, Anna K.; Nguyen, Doan H.; Dervan, Peter B.; Ptashne, Mark
CORPORATE SOURCE: Molecular Biology Program, Memorial Sloan-Kettering Cancer Center, Sloan-Kettering Institute, New York, NY, 10021, USA
SOURCE: Chemistry & Biology (2001), 8(6), 583-592
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Most transcriptional activators minimally comprise two functional modules, one for DNA binding and the other for activation. Several activators also bear an oligomerization region and bind DNA as dimers or higher order oligomers. In a previous study the authors substituted these domains of a protein activator with synthetic counterparts. An artificial transcriptional activator, 4.2 kDa in size, comprised of a DNA binding hairpin polyamide tethered to a 20 residue activating peptide (AH) was shown to stimulate promoter specific transcription. The question arises as to the general nature and the versatility of this minimal activator motif and whether smaller ligands can be designed which maintain potent activation function. Results: Here the authors have replaced the 20 amino acid AH peptide with eight or 16 residues derived from the activation domain of the potent viral activator VP16. The 16 residue activation module coupled to the polyamide activated transcription over two-fold better than the analogous AH conjugate. Altering the site of attachment of the activation module on the polyamide allowed redn. of the intervening linker from 36 atoms to eight without significant diminution of the activation potential. In this study the authors also exchanged the polyamide to target a different sequence without compromising the activation function further demonstrating the generality of this design. Conclusions: The polyamide activator conjugates described here represent a class of DNA binding ligands which are tethered to a second functional moiety, viz. an activation domain, that recruits elements of the endogenous transcriptional machinery. The results define the minimal structural elements required to construct artificial, small mol. activators. If such activators are cell-permeable and can be targeted to designated sites in the genome, this series of conjugates may then serve as a tool to study mechanistic aspects of transcriptional regulation and eventually to modulate gene expression relevant to human diseases.

CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 1, 6

IT **401901-37-9P 401901-38-0P**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DNA-binding hairpin polyamine conjugated to transcription activator VP16 peptide VP1; minimal structural elements for artificial transcriptional activators)

IT **401901-39-1P 401901-40-4P** 401901-58-4P
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP

(Preparation); USES (Uses)
(DNA-binding hairpin polyamine conjugated to transcription activator VP16 peptide VP2; minimal structural elements for artificial transcriptional activators)

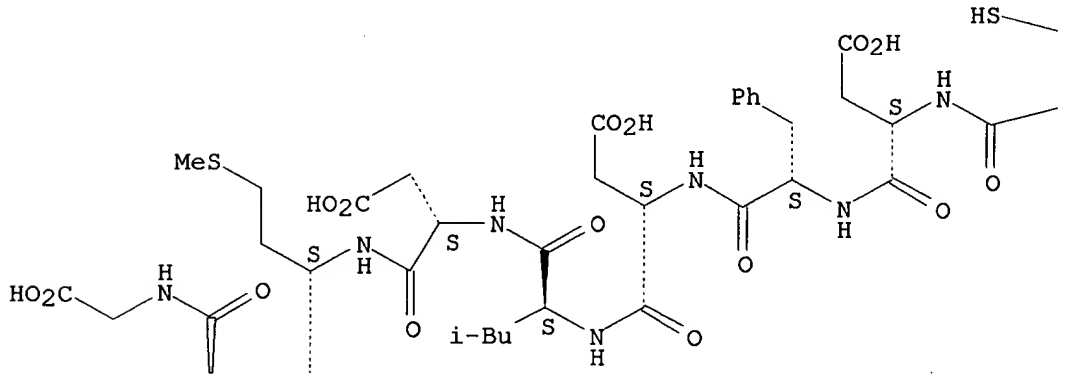
IT **401901-37-9P 401901-38-0P**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DNA-binding hairpin polyamine conjugated to transcription activator VP16 peptide VP1; minimal structural elements for artificial transcriptional activators)

RN 401901-37-9 HCAPLUS

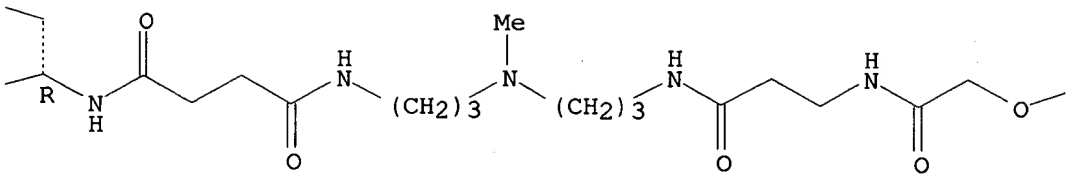
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-.beta.-alanyl-19-amino-5-oxo-3,10,13,16-tetraoxa-6-azanonadecanoyl-.beta.-alanyl-4-[[3-[(3-aminopropyl)methylamino]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

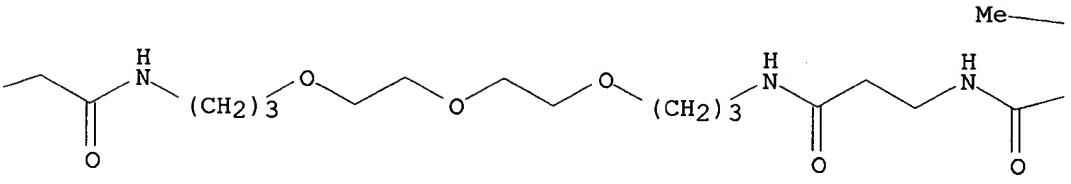
PAGE 1-A



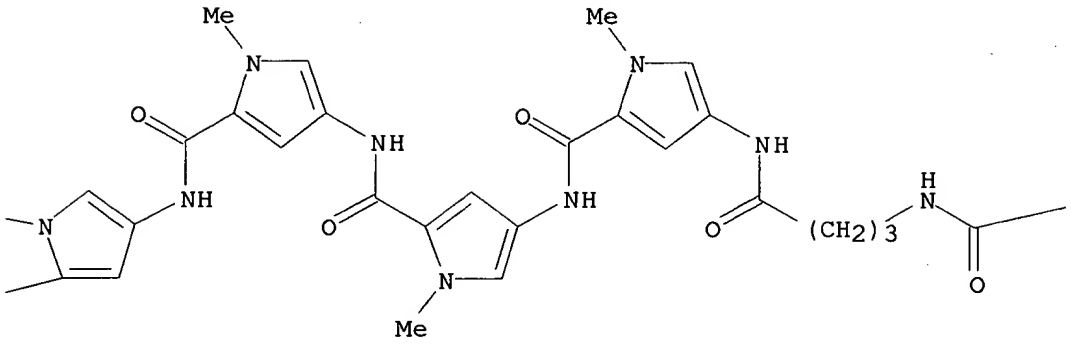
PAGE 1-B



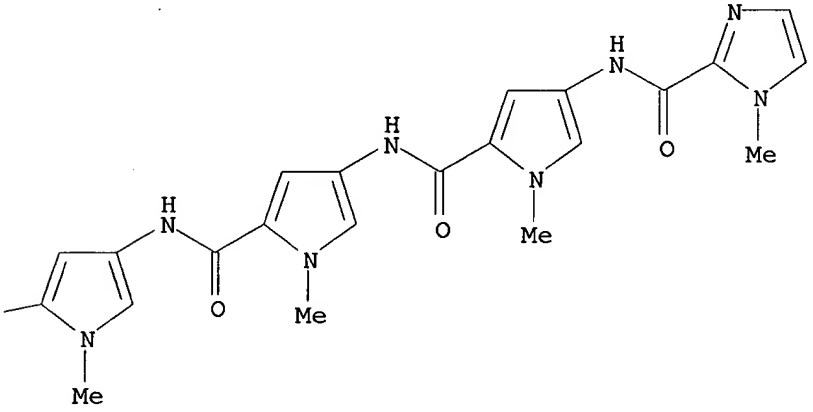
PAGE 1-C



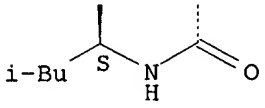
PAGE 1-D



PAGE 1-E



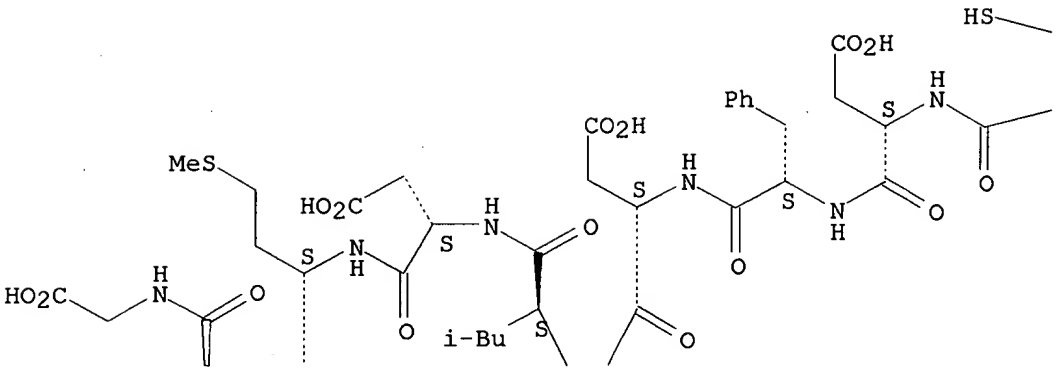
PAGE 2-A



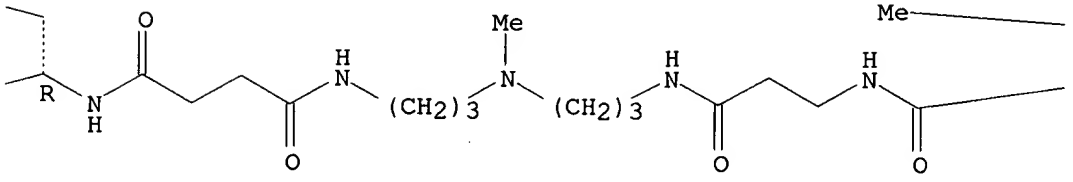
RN 401901-38-0 HCAPLUS
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-.beta.-alanyl-4-[[3-[(3-aminopropyl)methylamino]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

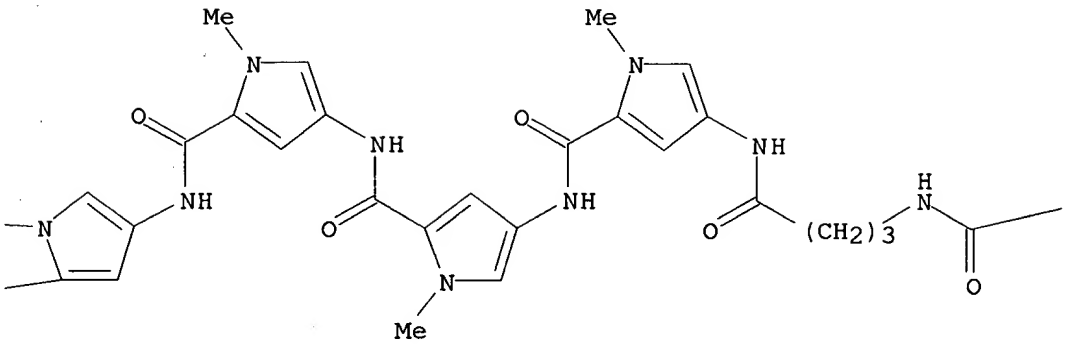
PAGE 1-A



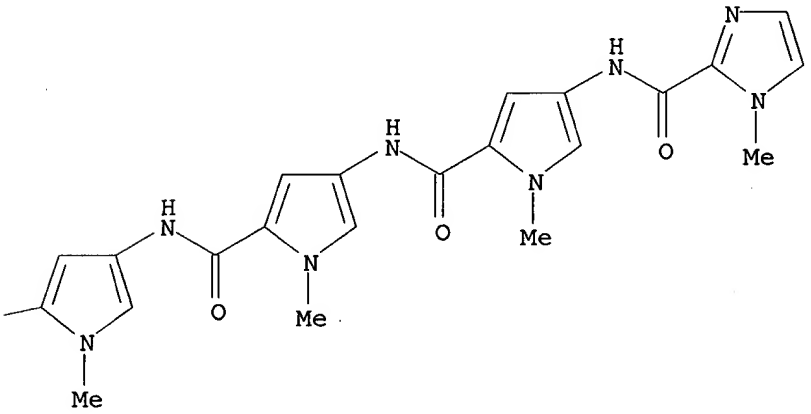
PAGE 1-B



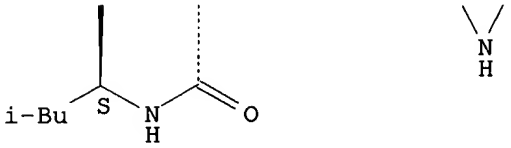
PAGE 1-C



PAGE 1-D



PAGE 2-A

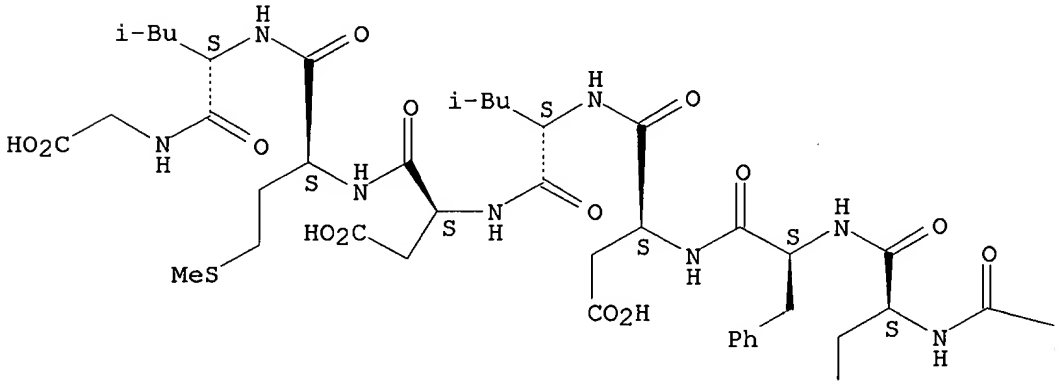


IT **401901-39-1P 401901-40-4P**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DNA-binding hairpin polyamine conjugated to transcription activator VP16 peptide VP2; minimal structural elements for artificial transcriptional activators)
RN 401901-39-1 HCAPLUS

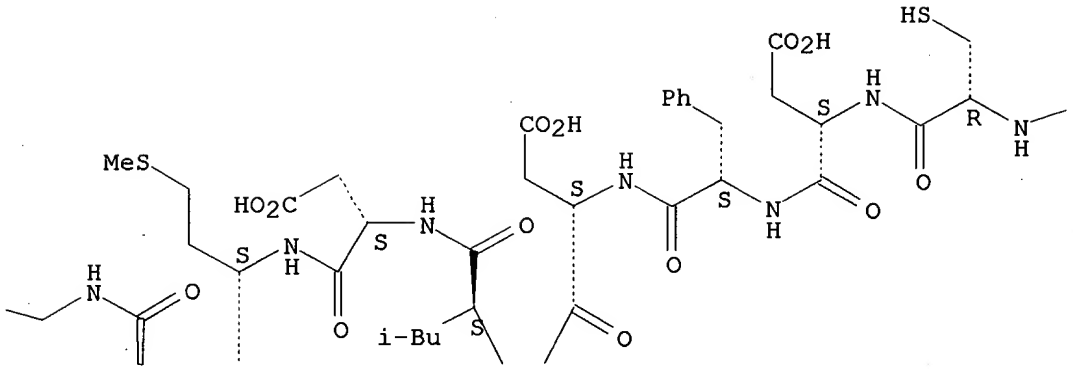
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-.beta.-alanyl-4-[[3-[(3-aminopropyl)methylamino]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

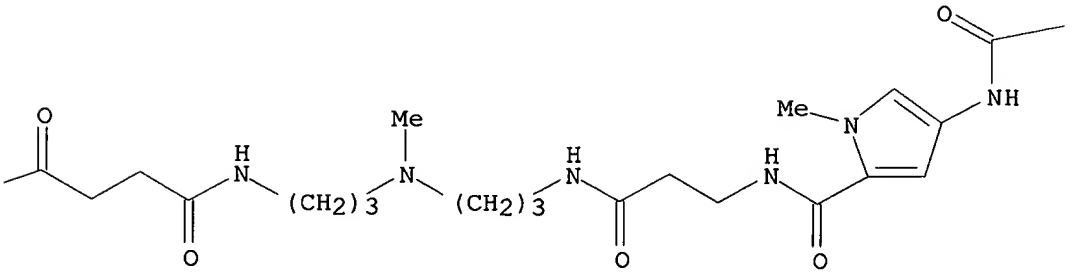
PAGE 1-A



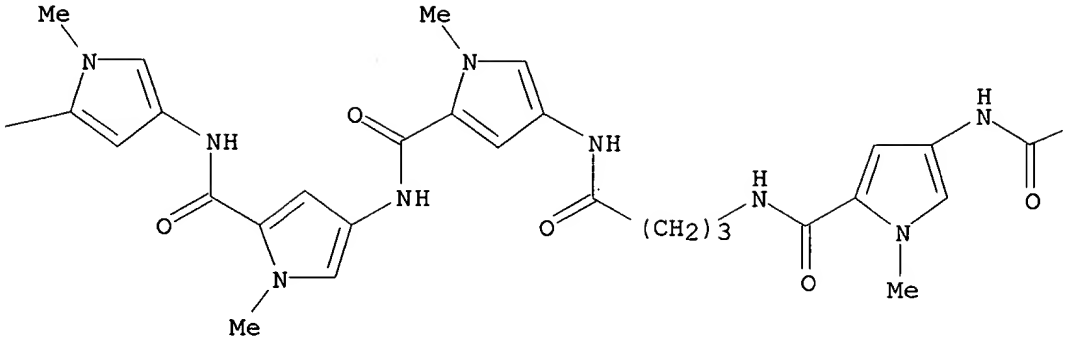
PAGE 1-B



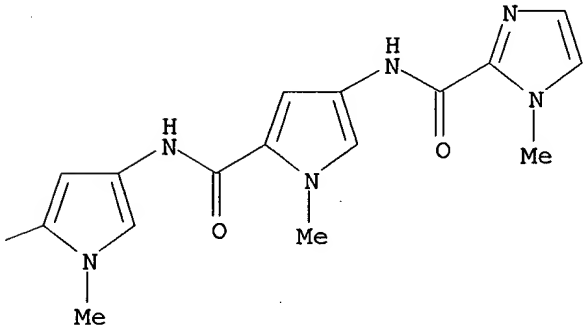
PAGE 1-C



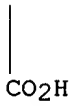
PAGE 1-D



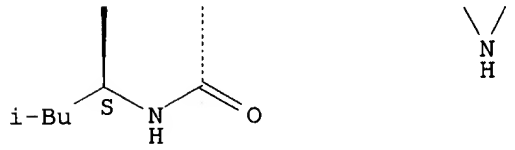
PAGE 1-E



PAGE 2-A



PAGE 2-B

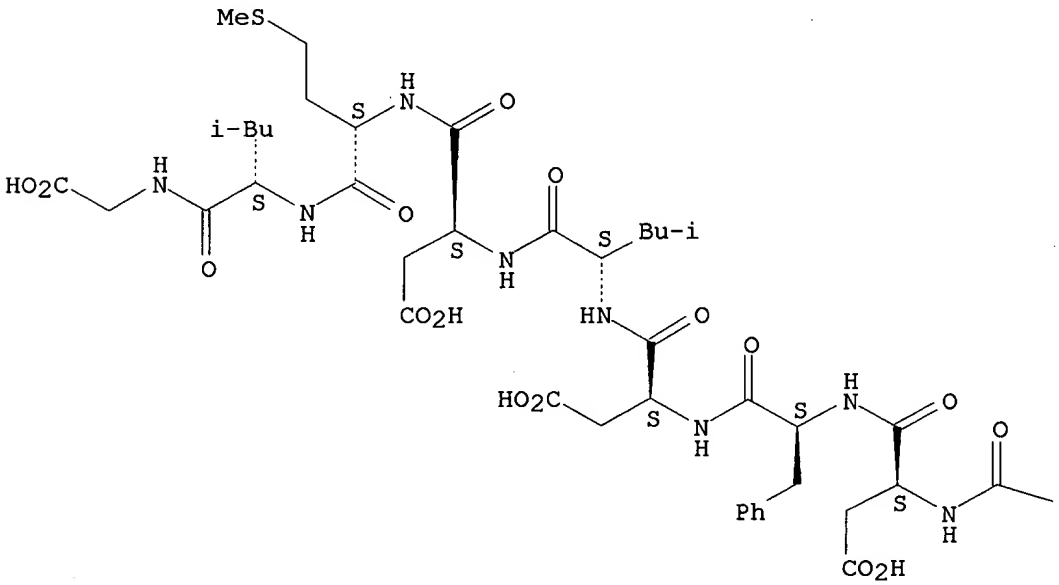


RN 401901-40-4 HCAPLUS
CN Glycine, 1-methyl-1H-imidazole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-

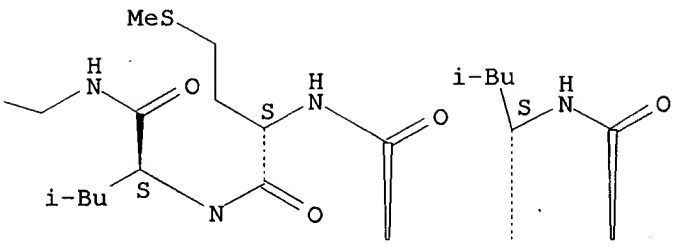
carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-aminobutanoyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-amino-1-methyl-1H-pyrrole-2-carbonyl-4-[[3-[4-amino-2-[[[3-[[3-(dimethylamino)propyl]amino]-3-oxopropyl]amino]carbonyl]-1H-pyrrol-1-yl]propyl]amino]-4-oxobutanoyl-L-cysteinyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-aspartyl-L-leucyl-L-.alpha.-aspartyl-L-methionyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



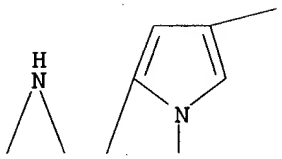
PAGE 1-B



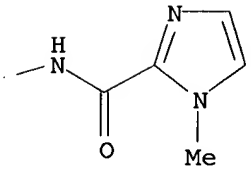
PAGE 1-C

Me

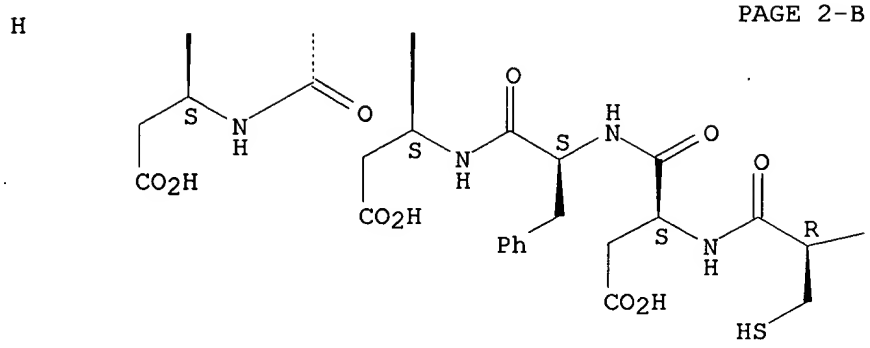
PAGE 1-D



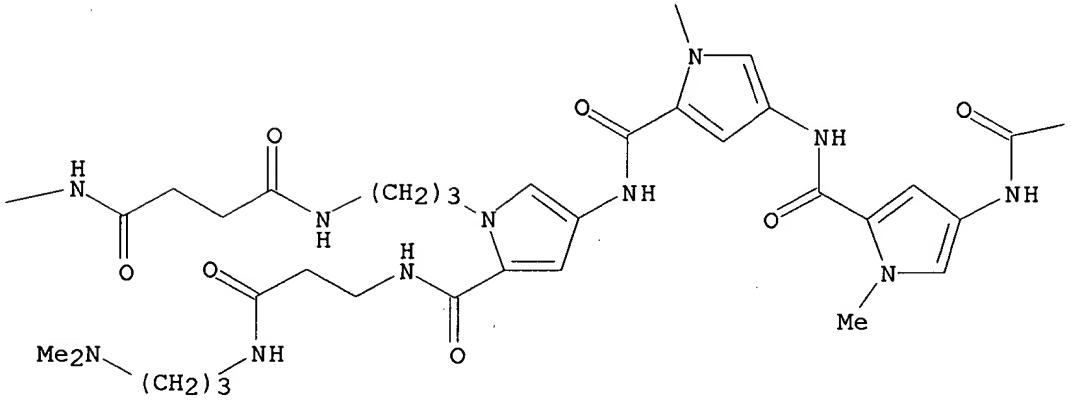
PAGE 1-E



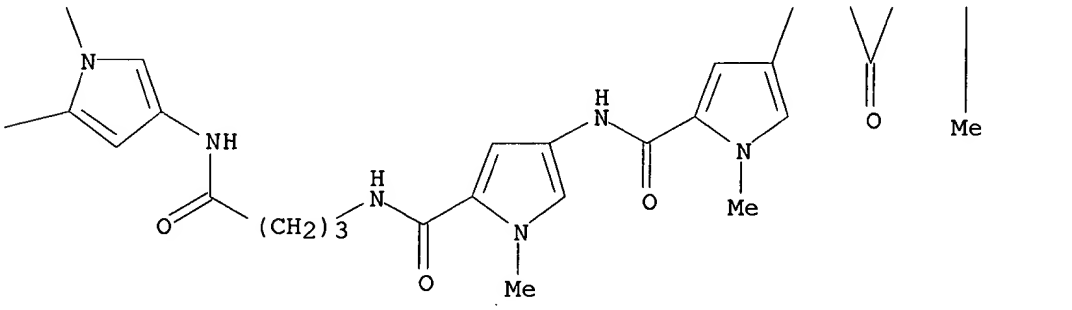
PAGE 2-B



PAGE 2-C



PAGE 2-D



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:802737 HCAPLUS
DOCUMENT NUMBER: 134:101174
TITLE: Solid-Phase Synthesis of a Radiolabeled, Biotinylated, and Farnesylated Cala2X Peptide Substrate for Ras- and

a-Mating Factor Converting Enzyme

AUTHOR(S): Dolence, E. Kurt; Dolence, Julia M.; Poulter, C. Dale
CORPORATE SOURCE: Department of Chemistry, University of Utah, Salt Lake City, UT, 84112-0850, USA

SOURCE: Bioconjugate Chemistry (2001), 12(1), 35-43
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Eukaryotic proteins with carboxyl-terminal Ca1a2 motifs undergo three posttranslational processing reactions (prenylation, endoproteolysis, and carboxymethylation). Two genes in yeast encoding Ca1a2X endoproteases, AFC1 and RCE1, have been identified. Rce1p is solely responsible for proteolysis of yeast Ras proteins. When proteolysis is blocked, localization of Ras2p to the outer membrane is impaired. The mislocalization of undermodified Ras in the cell suggests that Rce1p is an attractive target for cancer therapeutics. A biotinylated, farnesylated Ca1a2X peptide [[1-N-biotinyl-[13-N-succinimidyl-[S-(E,E-farnesyl)-L-cysteinyl]-L-valinyl-L-isoleucinyl-L-alanine]]-4,7,10-trioxatridecanediamine] (1) contg. a poly(ethylene glycol) linker was prepd. by solid-phase synthesis for use in an assay for Ca1a2X endoprotease activity that relies on the strong affinity of avidin for biotin. The peptide was radiolabeled in the penultimate step of the synthesis by cleavage of the biotinylated, farnesylated Ca1a2 precursor from Kaiser's oxime resin with [14C]-L-alanine Me ester. [14C]1 was a good substrate for yRce1p with KM = 1.3 .+-. 0.3 .mu.M. Anal. of the carboxyl terminal products by reverse phase HPLC confirmed that VIA was the only radioactive fragment released upon incubation of [14C]1 with a yeast membrane prepn. of recombinant yRce1p. The solid-phase methodol. developed using Kaiser's benzophenone oxime resin to synthesize [14C]1 should be generally applicable for peptides contg. sensitive side chains. In addn., introduction of the radiolabeled unit at the end of the synthesis mostly circumvents problems assocd. with handling radioactive materials.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7

IT **318510-97-3P 318511-03-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis of radiolabeled, biotinylated, and farnesylated Ca1a2X peptide substrate for Ras- and a-Mating factor converting enzyme)

IT 66024-28-0DP, resin-bound 318510-99-5DP, resin-bound 318511-01-2P
318511-02-3DP, resin-bound **318511-04-5P** 318511-05-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase synthesis of radiolabeled, biotinylated, and farnesylated Ca1a2X peptide substrate for Ras- and a-Mating factor converting enzyme)

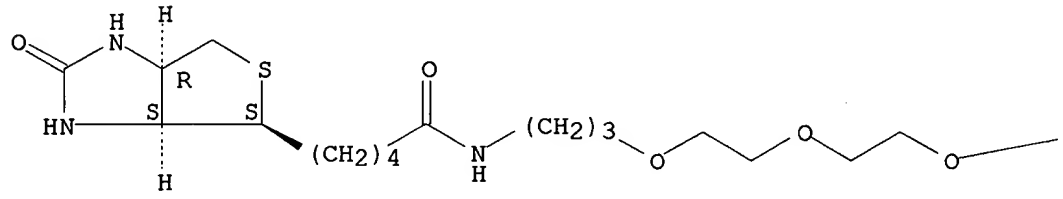
IT **318510-97-3P 318511-03-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase synthesis of radiolabeled, biotinylated, and farnesylated Ca1a2X peptide substrate for Ras- and a-Mating factor converting enzyme)

RN 318510-97-3 HCAPLUS

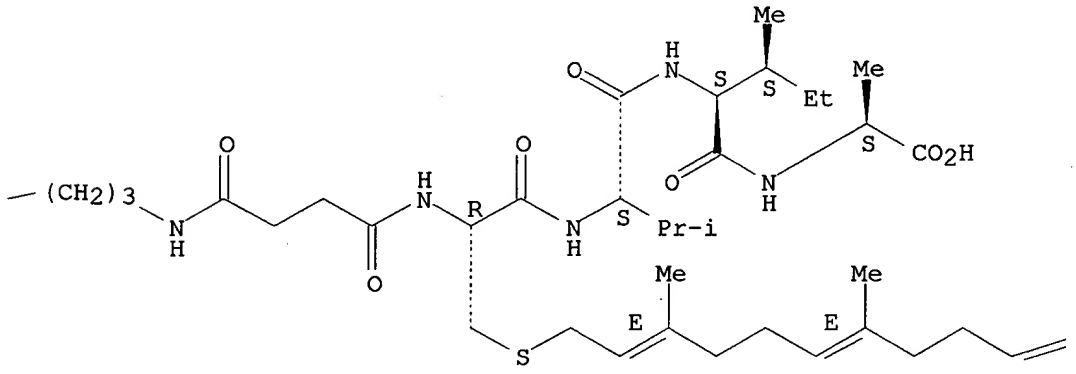
CN L-Alanine, N-[24-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1,4,20-trioxo-9,12,15-trioxa-5,19-diazatetracos-1-yl]-S-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-L-cysteinyl-L-valyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

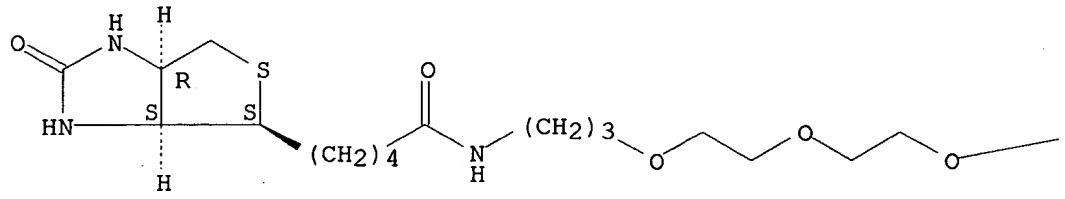


PAGE 1-C

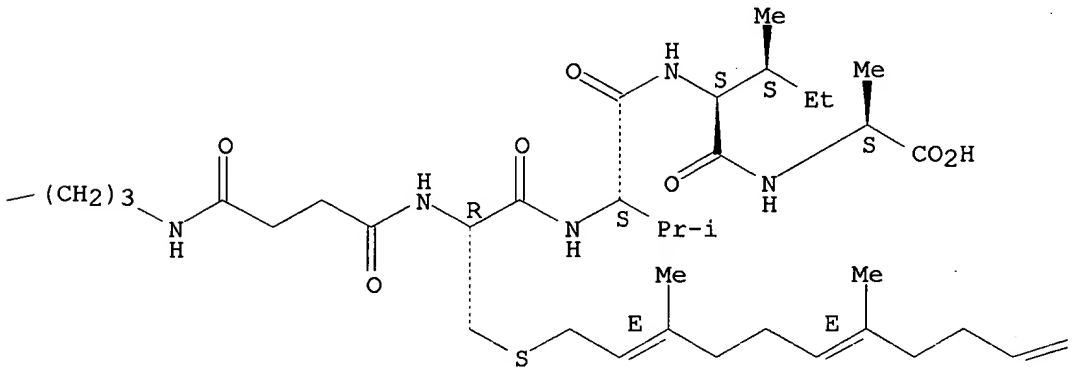
RN 318511-03-4 HCAPLUS
CN L-Alanine, N-[24-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1,4,20-trioxo-9,12,15-trioxa-5,19-diazatetracos-1-yl]-S-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-L-cysteinyl-L-valyl-L-isoleucyl-, labeled with carbon-14 (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



PAGE 1-C

=CMe2

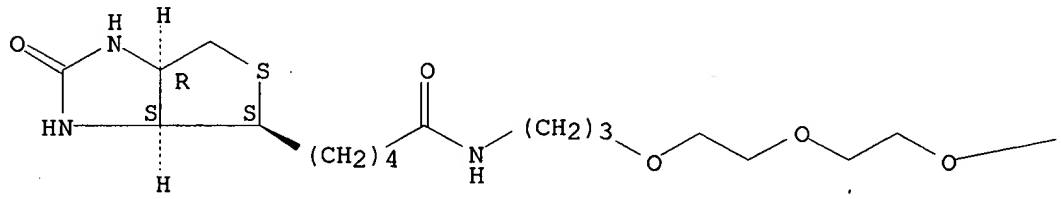
IT **318511-02-3DP**, resin-bound **318511-04-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase synthesis of radiolabeled, biotinylated, and farnesylated Cala2X peptide substrate for Ras- and a-Mating factor converting enzyme)

RN 318511-02-3 HCAPLUS

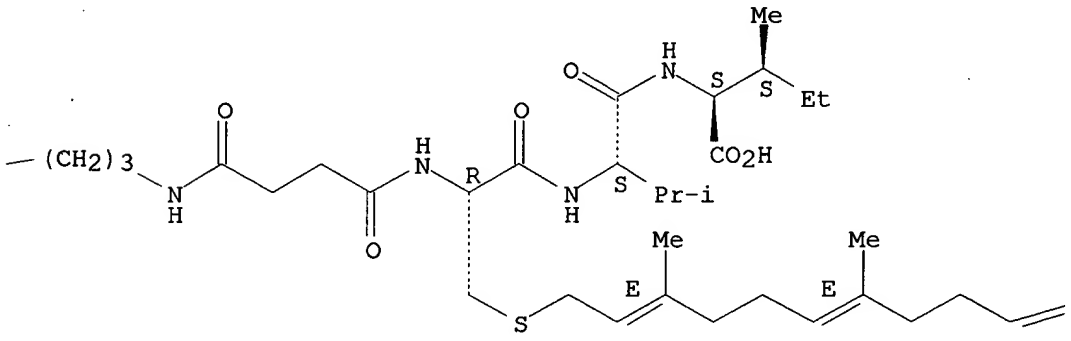
CN L-Isoleucine, N-[24-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1,4,20-trioxo-9,12,15-trioxa-5,19-diazatetracos-1-yl]-S-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-L-cysteinyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



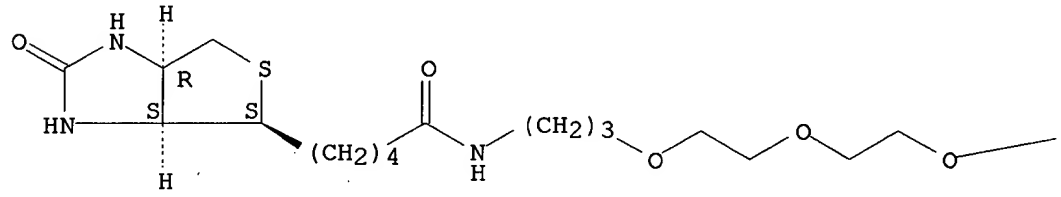
PAGE 1-C

=CMe2

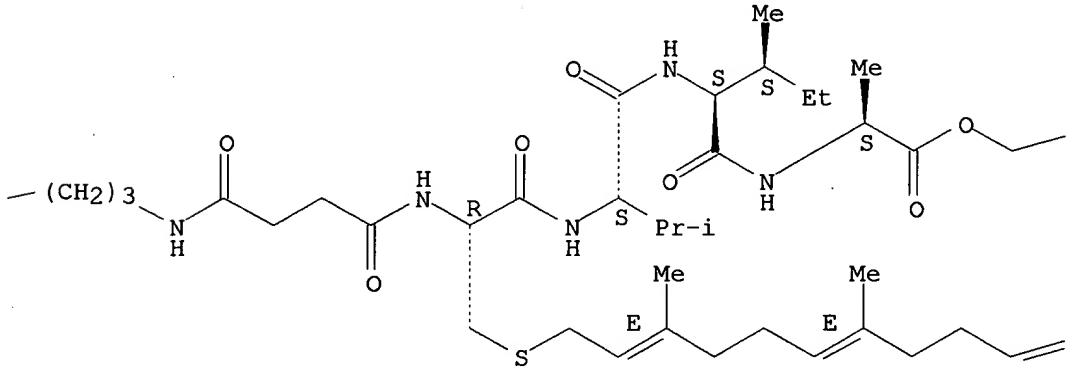
RN 318511-04-5 HCAPLUS
CN L-Alanine, N-[24-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1,4,20-trioxo-9,12,15-trioxa-5,19-diazatetracos-1-yl]-S-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl]-L-cysteinyl-L-valyl-L-isoleucyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

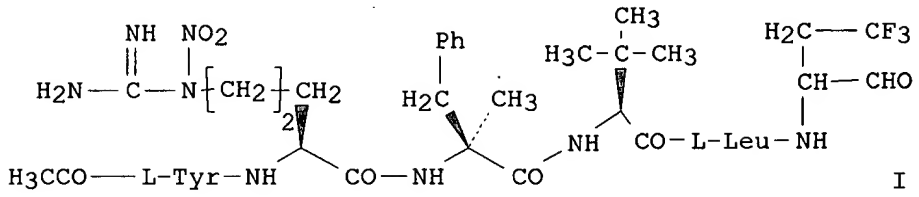


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:653384 HCAPLUS
DOCUMENT NUMBER: 131:257880
TITLE: Preparation and use of amino acid derivatives as anti-viral agents
INVENTOR(S): Attwood, Michael Richard; Hurst, David Nigel; Jones, Philip Stephen; Kay, Paul Brittain; Raynham, Tony Michael; Wilson, Francis Xavier
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19914474	A1	19991007	DE 1999-19914474	19990330
US 6372883	B1	20020416	US 1999-265617	19990310
FR 2777891	A1	19991029	FR 1999-3872	19990329
FR 2777891	B1	20030131		
GB 2337262	A1	19991117	GB 1999-7263	19990329
JP 11322789	A2	19991124	JP 1999-85092	19990329
ES 2160046	A1	20011016	ES 1999-627	19990329
ES 2160046	B1	20020516		
IT 1311994	B1	20020322	IT 1999-MI657	19990330

PRIORITY APPLN. INFO.: GB 1998-6815 A 19980330
OTHER SOURCE(S): MARPAT 131:257880
GI



I

AB Pentapeptides partially composed of modified or D-amino acids C-terminated with F3CCH2CH(NH)CHO or H3CCH2CH(NH)B(OH)2 amido groups [e.g. (I)] were synthesized, using resin-support methods, as anti-hepatitis drugs. In in vitro fluorescence tests against hepatitis C virus proteinase, I had IC50 0.044 .mu.M/L.

IC ICM C07K007-06
ICS A61K038-07

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

IT **244302-70-3P** 244302-83-8P 244302-87-2P 244302-91-8P
244303-28-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(reaction of in the synthesis of amino acid derivs. for use as anti-hepatitis agents)

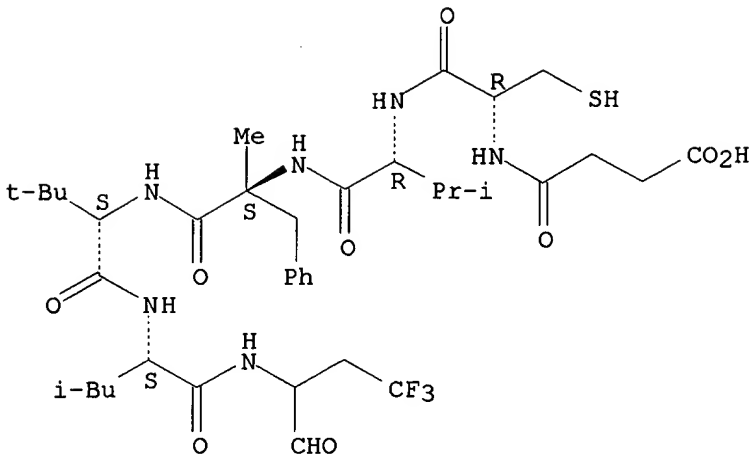
IT 244302-63-4DP, polymer-bound 244302-64-5P 244302-65-6P 244302-66-7P
244302-67-8P **244302-68-9P** 244302-69-0P 244302-71-4P
244302-72-5P 244302-73-6P 244302-74-7P 244302-75-8P 244302-76-9P
244302-77-0P 244302-78-1P 244302-79-2P 244302-80-5P 244302-81-6P
244302-82-7P 244302-84-9P 244302-85-0P 244302-86-1P 244302-88-3P
244302-89-4P 244302-90-7P 244302-92-9P 244302-93-0P 244302-94-1P
244302-95-2P 244302-96-3P 244302-97-4P 244302-98-5P 244302-99-6P
244303-00-2P 244303-01-3P 244303-02-4P 244303-03-5P 244303-04-6P
244303-05-7P 244303-06-8P 244303-07-9P 244303-08-0P 244303-09-1P
244303-10-4P 244303-11-5P 244303-12-6P 244303-13-7P 244303-14-8P
244303-15-9P 244303-16-0P 244303-17-1P 244303-18-2P 244303-19-3P
244303-20-6P 244303-21-7P 244303-22-8P 244303-23-9P 244303-24-0P
244303-25-1P 244303-26-2P 244303-27-3P 244303-29-5P 244303-30-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(reaction of in the synthesis of amino acid derivs. for use as anti-hepatitis agents)

IT **244302-70-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(reaction of in the synthesis of amino acid derivs. for use as anti-hepatitis agents)

RN 244302-70-3 HCAPLUS

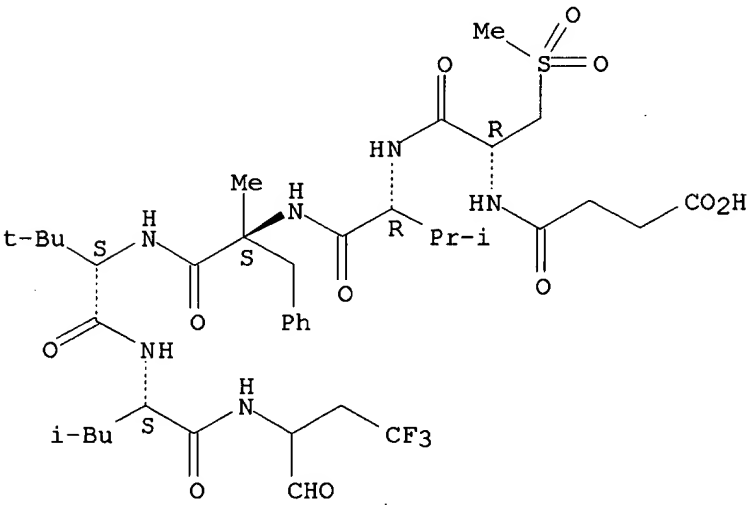
CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-L-cysteinyl-D-valyl-.alpha.-methyl-L-phenylalanyl-3-methyl-L-valyl-N-(3,3,3-trifluoro-1-formylpropyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **244302-68-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(reaction of in the synthesis of amino acid derivs. for use as anti-hepatitis agents)
RN 244302-68-9 HCAPLUS
CN L-Leucinamide, N-(3-carboxy-1-oxopropyl)-3-(methylsulfonyl)-L-alanyl-D-valyl-.alpha.-methyl-L-phenylalanyl-3-methyl-L-valyl-N-(3,3,3-trifluoro-1-formylpropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:578886 HCAPLUS
DOCUMENT NUMBER: 132:666
TITLE: Dimers of bradykinin and substance P antagonists as potential anti-cancer drugs
AUTHOR(S): Stewart, J. M.; Gera, L.; Chan, D. C.
CORPORATE SOURCE: Department of Biochemistry, University of Colorado

Medical School, Denver, CO, 80262, USA
SOURCE: Peptide Science: Present and Future, Proceedings of the International Peptide Symposium, 1st, Kyoto, Nov. 30-Dec. 5, 1997 (1999), Meeting Date 1997, 731-732. Editor(s): Shimonishi, Yasutsugu. Kluwer: Dordrecht, Neth.
CODEN: 68BYA5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The authors report dimers of bradykinin (BK) and substance P (SP) antagonists and heterodimers of SP and BK antagonists that are potent selectively cytotoxic agents for small cell lung cancer (SCLC). Although straight-chain analogs of SP and bombesin have shown toxicity against SCLC, none of the simple BK antagonists were toxic to cells, although they were very effective for inhibition of BK-evoked elevation of intracellular free calcium in SCLC cultures. Typical of this behavior is B-9430, a very potent 'third-generation' BK antagonist which is active against both B1 and B2 BK receptors and shows a long half-life in vivo. When this antagonist was crosslinked by suberimide at the N-terminus (B-201), potent cytoxic activity was found. Dimers of 'first-generation' BK antagonists, such as CP-127, were introduced by investigators at Cortech , and while they are quite potent antagonists in many BK assays, were not cytotoxic. When the linker in CP-127 was moved to the N-terminus of the dimer (B-197) significant toxicity was found. Even dimers of the potent 'second-generation' Hoechst antagonist HOE-140 showed only low cytotoxicity against SCLC. Orosz et al. reported that a pseudopeptide substance P antagonist (B-237) was active against SCLC. The authors confirmed this activity, and found that neither a homodimer (B-240) nor a heterodimer of this peptide with the best BK antagonist (B-215) showed increased cytotoxicity. Certain of these new dimers are toxic to SCLC lines that show multidrug resistance phenotypes, testifying to the different mechanism of toxicity of these agents. Preliminary studies indicate that these new dimers act by stimulation of apoptosis in SCLC cells. Peptide dimer B-201 inhibited the growth of SCLC cell line SHP-77 when implanted s.c. in athymic (nude) mice. These dimers offer a new avenue for anti-cancer drug development.

CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 1

IT 157967-60-7, CP-127 180981-09-3 215713-39-6 215713-84-1
250784-51-1 250784-52-2 250784-53-3, B 240 250784-54-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dimers of bradykinin and substance P antagonists as potential anti-cancer drugs)

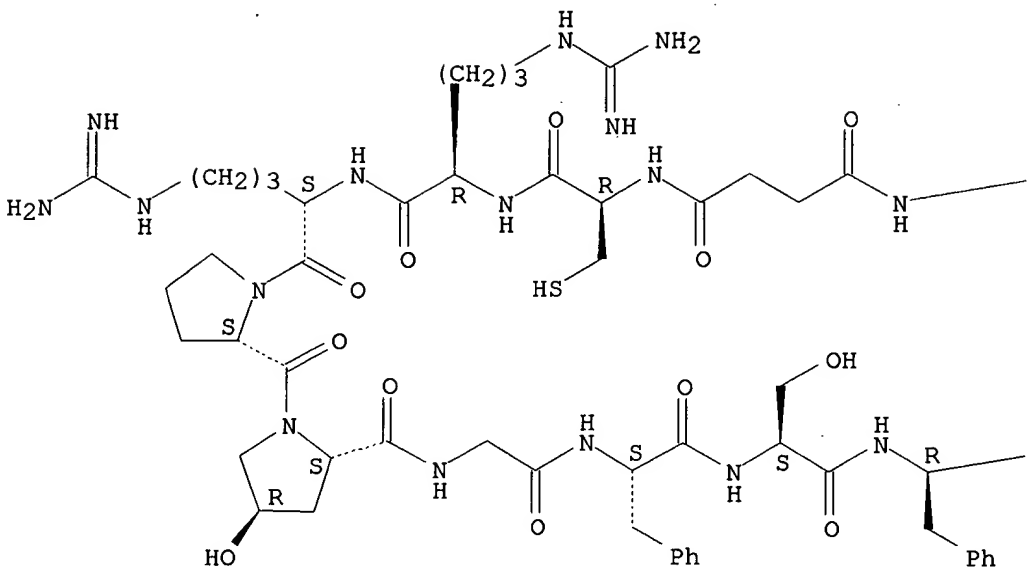
IT **250784-51-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dimers of bradykinin and substance P antagonists as potential anti-cancer drugs)

RN 250784-51-1 HCAPLUS

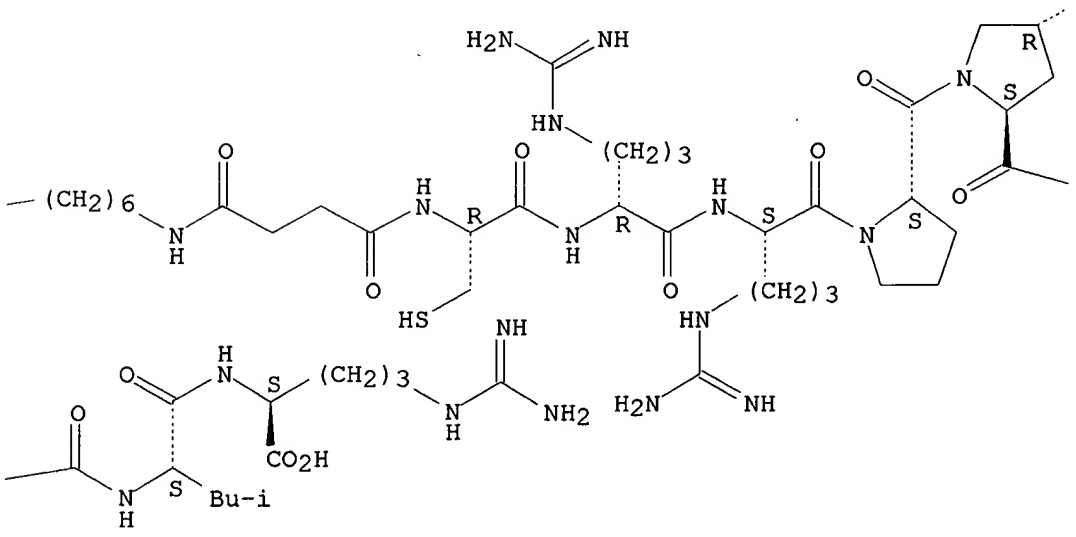
CN L-Arginine, 1,1'-[1,6-hexanediylbis[imino(1,4-dioxo-4,1-butanediyl)]]bis[L-cysteinyl-D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-seryl-D-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

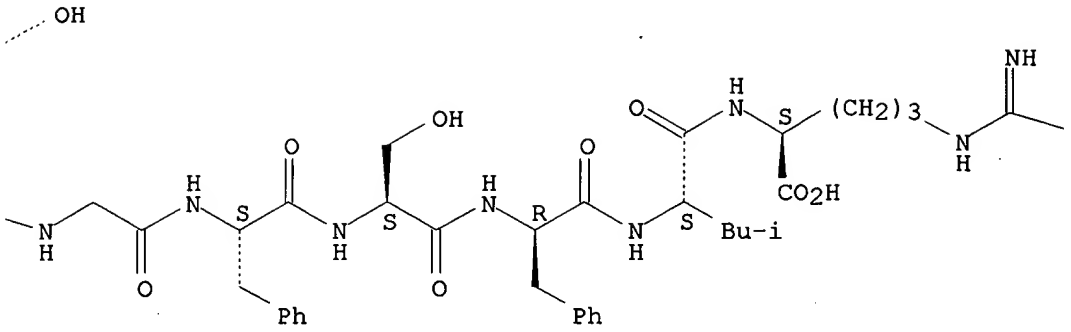
PAGE 1-A



PAGE 1-B



PAGE 1-C



PAGE 1-D

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:682515 HCAPLUS
DOCUMENT NUMBER: 129:286004
TITLE: Peptides agonists of insulin-like growth factor that inhibit interaction with IGF-binding proteins without affecting binding to the receptor
INVENTOR(S): Clark, Ross G.; Lowman, Henry B.; Robinson, Iain C. A. F.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9845427	A2	19981015	WO 1998-US6514	19980331
WO 9845427	A3	19990107		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6121416	A	20000919	US 1997-825852	19970404

AU 9869470 A1 19981030 AU 1998-69470 19980331
AU 732989 B2 20010503
EP 972020 A1 20000119 EP 1998-915236 19980331
EP 972020 B1 20020925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002510194 T2 20020402 JP 1998-542894 19980331
AT 224951 E 20021015 AT 1998-915236 19980331
EP 1251137 A2 20021023 EP 2002-14880 19980331
EP 1251137 A3 20030416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
ES 2183344 T3 20030316 ES 1998-915236 19980331
PRIORITY APPLN. INFO.: US 1997-825852 A 19970404
EP 1998-915236 A3 19980331
WO 1998-US6514 W 19980331

AB Peptides that act as agonists of insulin-like growth factor (IGF) by inhibiting binding of the factor to IGF-binding proteins but that do not inhibit IGF binding to its receptor are described. These agonist peptides can be used to increase serum and tissue levels of active IGFs in a mammal. These peptides can also lower plasma insulin secretion, lower plasma growth hormone levels, or lower blood glucose levels. Injection of one of these analogs 100 .mu.g into 240-250 g rats resulted in an immediate (within 10 mins) and persistent (>60 min) lowering of plasma insulin levels by 25% with a concomitant significant fall in blood glucose. In a rat diabetes model, similar effects were found. Long term administration of the agonist to hypophysectomized rats also increased the effectiveness of growth hormone, leading to increased organ mass and enlargement of epiphyseal plates to near max. thicknesses. A large set of such peptides was identified by screening a phage display library.

IC ICM C12N015-11
ICS C07K019-00; A61K038-30; C07K007-08; C07K014-00; C07K016-18; C07K007-00; G01N033-68
CC 1-10 (Pharmacology)
Section cross-reference(s): 2

IT 214203-55-1 214203-56-2 214203-57-3 214203-58-4 214203-59-5
214203-60-8D, substitution analogs 214203-61-9D, substitution analogs
214203-62-0D, substitution analogs 214203-63-1 214203-63-1D,
substitution analogs 214203-64-2D, substitution analogs 214203-65-3D,
substitution analogs 214203-66-4D, substitution analogs 214203-67-5D,
substitution analogs 214203-68-6D, substitution analogs 214203-69-7
214203-70-0 214203-71-1 214203-72-2 214203-73-3 214203-74-4
214203-75-5 214203-76-6 214203-77-7 214203-78-8 214203-79-9
214203-80-2 214203-81-3 214203-82-4 214203-83-5 214203-84-6
214203-85-7 214203-86-8 214203-87-9 214203-88-0 214203-89-1
214203-90-4 214203-91-5 214203-92-6 214203-93-7 214203-94-8
214203-95-9 214203-96-0 214203-97-1 214203-98-2 214203-99-3
214204-00-9 214204-01-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IGF agonist peptide; peptides agonists of insulin-like growth factor that inhibit interaction with IGF-binding proteins without affecting binding to receptor)

IT **214204-00-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

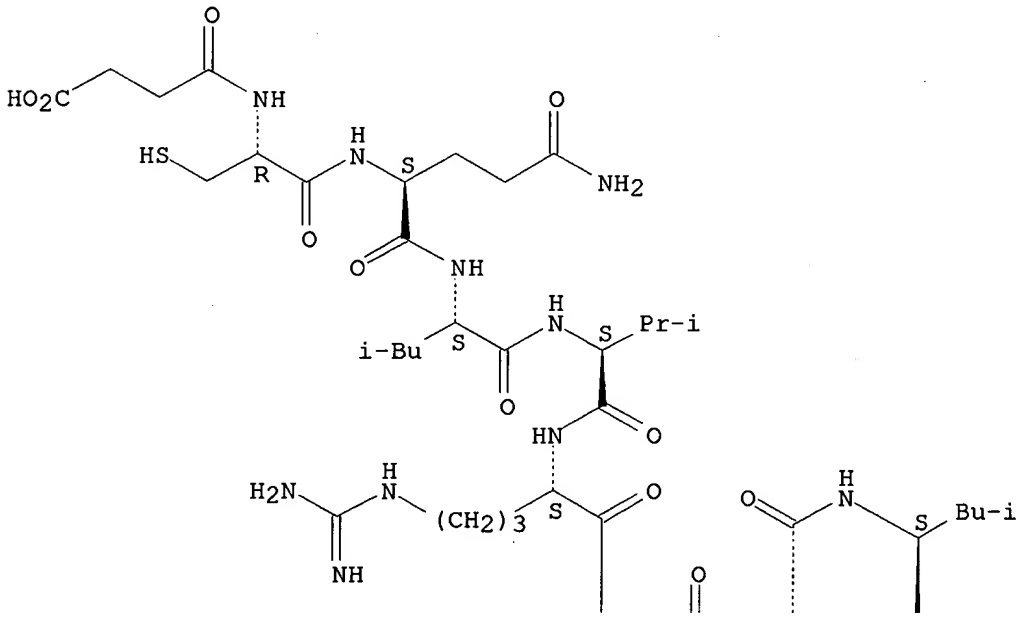
(IGF agonist peptide; peptides agonists of insulin-like growth factor that inhibit interaction with IGF-binding proteins without affecting binding to receptor)

RN 214204-00-9 HCAPLUS

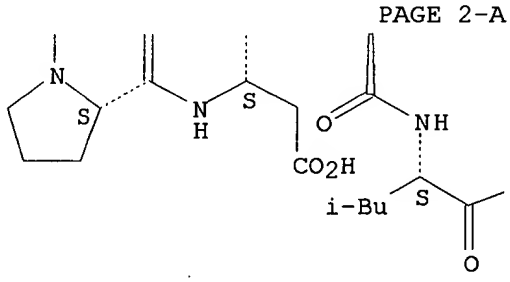
CN L-Glutamamide, N-(3-carboxy-1-oxopropyl)-L-cysteinyl-L-glutaminyl-L-leucyl-L-valyl-L-arginyl-L-prolyl-L-.alpha.-aspartyl-L-leucyl-L-leucyl-L-leucyl-L-cysteinyl- (9CI) (CA INDEX NAME)

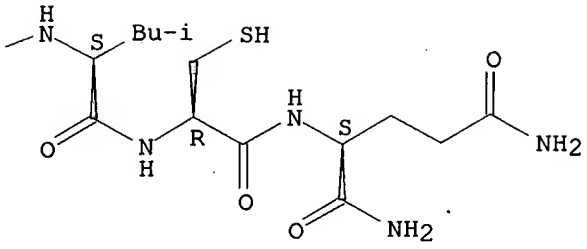
Absolute stereochemistry.

PAGE 1-A



PAGE 2-A





L9 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:456231 HCAPLUS
DOCUMENT NUMBER: 125:123737
TITLE: Polymer compound and coated particle composition
INVENTOR(S): Zalipsky, Samuel; Martin, Francis J.
PATENT ASSIGNEE(S): Liposome Technology, Inc., USA
SOURCE: U.S., 24 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5534259	A	19960709	US 1993-89086	19930708

PRIORITY APPLN. INFO.: US 1993-89086 19930708

AB A compn. of polymer-coated particles, and a polymer compd. used in forming the particles are disclosed. The polymer compd. is composed of a hydrophilic polymer attached to a lipophilic moiety through a linking segment which contains chem. groups through which the compd. can be crosslinked to other such compds. The particles in the compn. are prepd. by forming lipid structures contg. ordered arrays of the polymer compds., and crosslinking the compds. through their chem. groups. The particles are used for parenteral administration of a pharmaceutical compd. which is entrapped in the particles.

IC ICM A61K009-127
ICS A01N025-26; A01N025-28

NCL 424450000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 38

IT 179823-42-8P 179823-43-9P 179823-46-2P **179823-47-3P**
179823-50-8P 179823-51-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polymer compd. and coated particle compns.)

IT 25322-68-3DP, polymer compd. contg. 179823-44-0P **179823-48-4P**
179823-52-0P 179823-53-1DP, reaction products with amino group- and mercapto group-contg. polymers
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

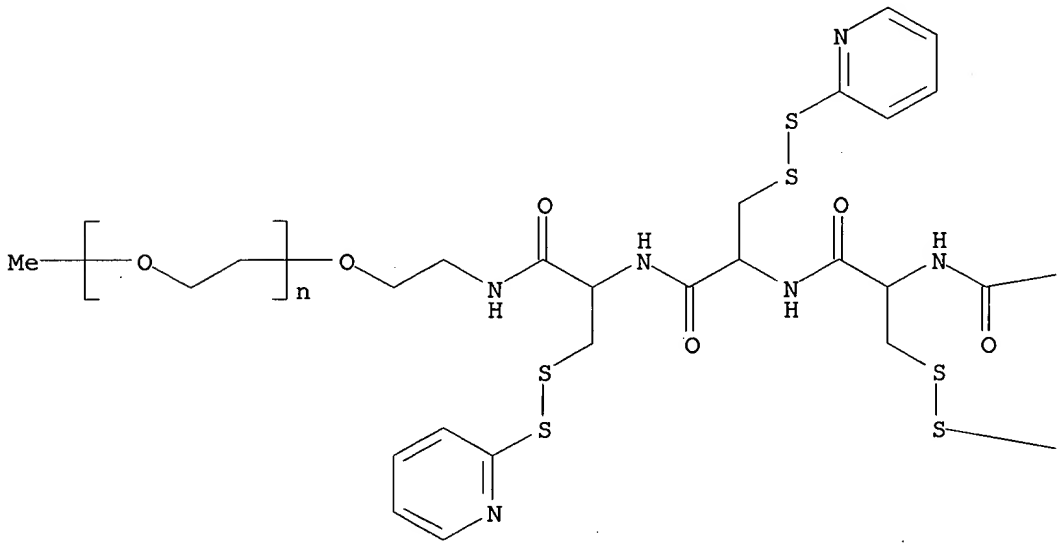
study); PREP (Preparation); USES (Uses)
(polymer compd. and coated particle compns.)

IT **179823-47-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polymer compd. and coated particle compns.)

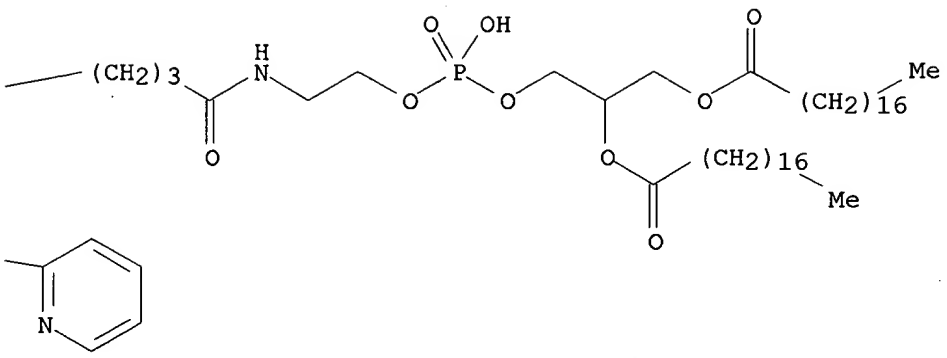
RN 179823-47-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy-, ether with N-[10-hydroxy-10-oxido-1,5,16-trioxo-13-[(1-oxooctadecyl)oxy]-9,11,15-trioxa-6-aza-10-phosphatritriacont-1-yl]-3-(2-pyridinyldithio)-L-alanyl-3-(2-pyridinyldithio)-L-alanyl-N-(2-hydroxyethyl)-3-(2-pyridinyldithio)-L-alaninamide (9CI) (CA INDEX NAME)

PAGE 1-A

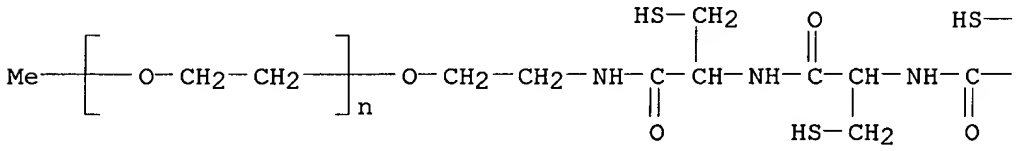


PAGE 1-B

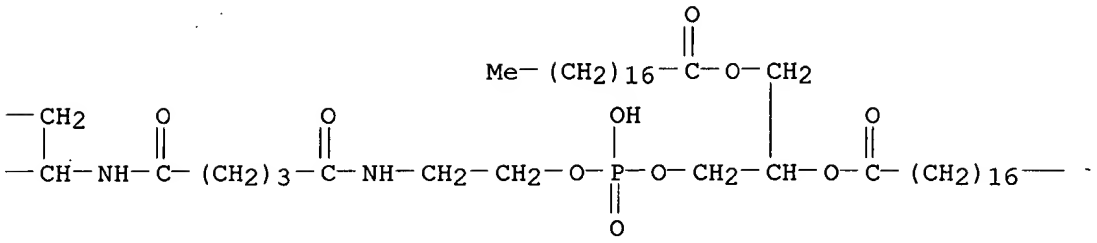


IT **179823-48-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymer compd. and coated particle compns.)
RN 179823-48-4 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy-, ether with N-[10-hydroxy-10-oxido-1,5,16-trioxo-13-[(1-oxooctadecyl)oxy]-9,11,15-trioxa-6-aza-10-phosphatritriacont-1-yl]-L-cysteinyl-L-cysteinyl-N-(2-hydroxyethyl)-L-cysteinamide (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



PAGE 1-C

—Me

L9 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:128288 HCAPLUS
DOCUMENT NUMBER: 120:128288
TITLE: The glutamyl binding site of trypanothione reductase from Crithidia fasciculata: enzyme kinetic properties of .gamma.-glutamyl-modified substrate analogs
AUTHOR(S): El-Waer, Abdussalam F.; Smith, Keith; McKie, James H.; Benson, Timothy; Fairlamb, Alan H.; Douglas, Kenneth T.
CORPORATE SOURCE: Department of Pharmacy, University of Manchester, Manchester, UK
SOURCE: Biochimica et Biophysica Acta (1993), 1203(1), 93-8
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Trypanothione reductase, central to the redox defense systems of parasitic trypanosomes and leishmanias, is sufficiently different in its substrate-specificity from mammalian glutathione reductase to represent an attractive target for chemotherapeutic intervention. Previous studies of the physiol. substrates trypanothione (N1,N8-bis(glutathionyl)spermidine) and N1-glutathionylspermidine disulfide established that the spermidine moiety of these substrates can be replaced by the 3-dimethyl-propylamide group (N1-glutathionyl-N3-dimethyl-propylamide). With this modification, the specificity for the .gamma.-glutamyl moiety of the substrate was examd. Kinetic anal. of a series of substrate analogs indicated that neither the .alpha.-carboxylate or .alpha.-amino functions of the L-.gamma.-glutamyl group is essential for recognition, since this group could be replaced by uncharged benzyloxycarbonyl or t-butyloxycarbonyl groups with relative catalytic efficiencies (kcat/Km) of 58 and 11%, resp., of N1-glutathionyl-N3-dimethylpropylaminedisulfide. Other substitutions are less well tolerated (e.g., .beta.-L-aspartyl or

aminobutyryl) or not at all (e.g., glutaryl). These findings are discussed in relation to the structural model of TR from Trypanosoma congolense. The successful structural replacements achieved have potential application for drug delivery.

CC 7-3 (Enzymes)
Section cross-reference(s): 63

IT 108081-80-7 137888-43-8 148333-09-9 148333-10-2 **148333-12-4** 148333-14-6 148333-16-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with trypanothione reductase of Crithidia fasciculata, kinetics of, structure in relation to)

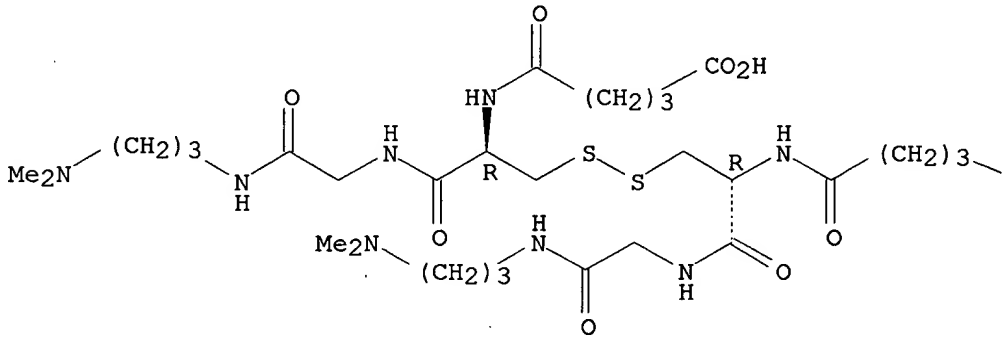
IT **148333-12-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with trypanothione reductase of Crithidia fasciculata, kinetics of, structure in relation to)

RN 148333-12-4 HCAPLUS

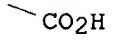
CN Glycinamide, N-(4-carboxy-1-oxobutyl)-L-cysteinyl-N-[3-(dimethylamino)propyl]-, bimol. (1.fwdarw.1')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L9 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:423375 HCAPLUS
DOCUMENT NUMBER: 119:23375
TITLE: Synthesis of substrate analogs for trypanothione reductase
AUTHOR(S): El-Waer, Abdussalam F.; Benson, Timothy; Douglas, Kenneth T.
CORPORATE SOURCE: Dep. Pharm., Univ. Manchester, Manchester, UK

SOURCE: International Journal of Peptide & Protein Research (1993), 41(2), 141-6
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and chem. characterization of a range of substrate analogs for trypanothione reductase are described, with the spermidine portion of trypanothione replaced by the 3-dimethylaminopropylamide moiety. Using 1-hydroxybenzotriazole/N-hydroxysuccinimide coupling, products were obtained which had a range of replacements of the .gamma.-glutamyl groups of the enzyme substrate. The materials were characterized by fast-protein liq. chromatog., 1H/13C NMR spectroscopy, and fast atom bombardment mass spectroscopy.

CC 7-3 (Enzymes)

IT 108081-80-7P 148333-08-8P 148333-09-9P 148333-11-3P
148333-12-4P 148333-13-5P 148333-14-6P 148333-15-7P
148333-16-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as trypanothione reductase substrate)

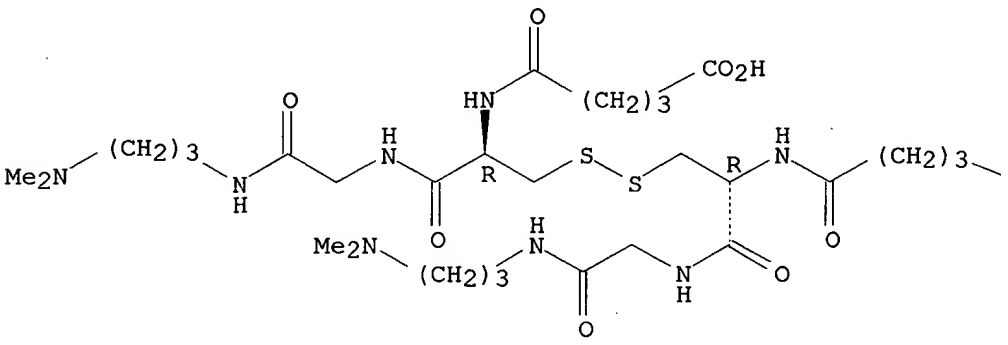
IT **148333-12-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as trypanothione reductase substrate)

RN 148333-12-4 HCAPLUS

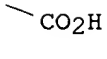
CN Glycinamide, N-(4-carboxy-1-oxobutyl)-L-cysteinyl-N-[3-(dimethylamino)propyl]-, bimol. (1.fwdarw.1')-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L9 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:46310 HCAPLUS
DOCUMENT NUMBER: 116:46310
TITLE: Polypeptide-drug conjugates for cell targetting
INVENTOR(S): Miles-Brown, Jonathan
PATENT ASSIGNEE(S): Oxford Virology PLC, UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9112021	A2	19910822	WO 1991-GB215	19910213
WO 9112021	A3	19911212		
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9172178	A1	19910903	AU 1991-72178	19910213

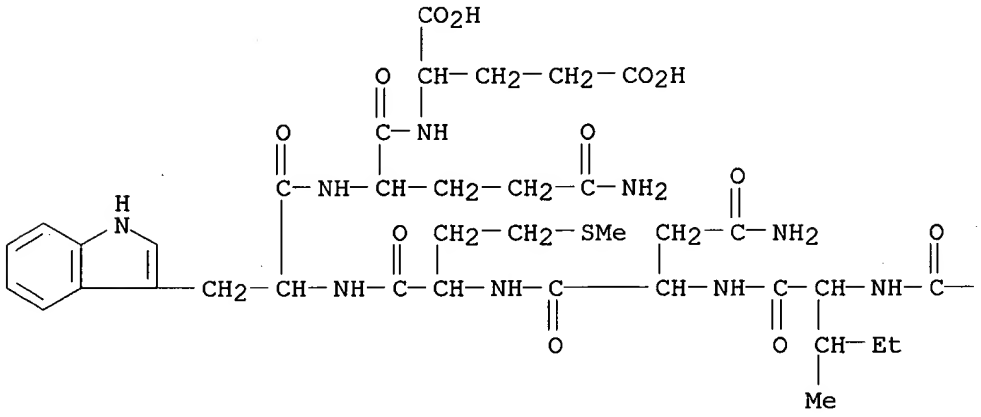
PRIORITY APPLN. INFO.: GB 1990-3257 19900213
GB 1990-6500 19900323
WO 1991-GB215 19910213
OTHER SOURCE(S): MARPAT 116:46310

AB A therapeutically active substance is covalently linked to a low mol. wt. polypeptide. The polypeptide comprises an amino acid sequence which is recognized by a recognition site of a receptor of a selected cell, group of cells or organs. The therapeutic agent is active itself and/or is convertible at or within the selected cell, group of cells or organ to a form which is therapeutically active. Target cells are CD4 lymphocytes, and the amino acid sequence comprises a sequence which is recognized by the CD4 receptor. 5'-O-Succinoyl AZT (prepn. is given) was reacted with Cys-Arg-Ile-Lys-Gln-Phe-Ile-Asn-Met-Trp-Gln-Glu (I) according to the Merrifield method to obtain I-succinyl AZT.

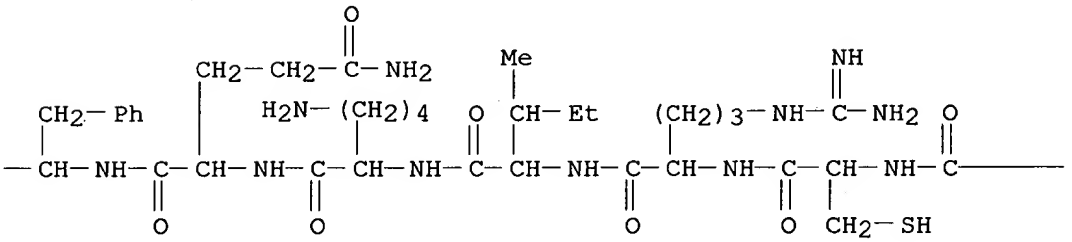
IC ICM A61K047-48
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 34
IT 51-21-8DP, 5-Fluorouracil, conjugates with polypeptides 7481-89-2DP, 2',3'-Dideoxycytidine, conjugates with polypeptides 30516-87-1DP, 3'-Deoxy-3'-azidothymidine, conjugates with polypeptides 59277-89-3DP, Acyclovir, conjugates with polypeptides 59298-42-9P 69655-05-6DP, 2',3'-Dideoxyinosine, conjugates with polypeptides 106060-83-7P 117205-65-9DP, conjugates with drugs 138320-99-7DP, conjugates with drugs 138321-00-3DP, conjugates with drugs 138321-01-4DP, conjugates with drugs 138321-02-5DP, conjugates with drugs 138321-03-6DP, conjugates with drugs 138321-04-7DP, conjugates with drugs 138321-05-8DP, conjugates with drugs 138321-06-9DP, conjugates with drugs 138321-07-0DP, conjugates with drugs 138321-08-1DP, conjugates with drugs 138321-09-2DP, conjugates with drugs 138321-10-5DP, conjugates with drugs **138321-11-6P** 138321-13-8P
RL: PREP (Preparation)
(prepn. of, for cell targetting)
IT **138321-11-6P**
RL: PREP (Preparation)
(prepn. of, for cell targetting)
RN 138321-11-6 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N-[N2-[N-[N-[N2-[N2-[N-[N2-[N-(3-carboxy-1-oxopropyl)-L-cysteinyl]-L-arginyl]-L-isoleucyl]-L-lysyl]-L-glutaminyl]-L-phenylalanyl]-L-isoleucyl]-L-asparaginyl]-L-methionyl]-L-tryptophyl]-L-

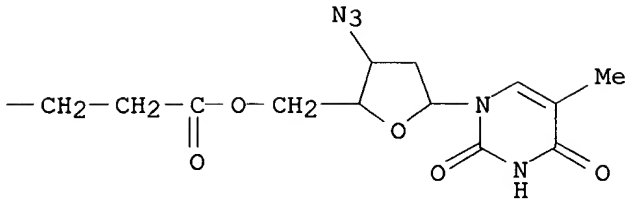
glutaminyl]-, N.fwdarw.5'-ester with 3'-azido-2',3'-dideoxythymidine (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B





L9 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:612642 HCAPLUS
DOCUMENT NUMBER: 113:212642
TITLE: Synthesis of cyclic peptides on solid support. Application to analogs of hemagglutinin of influenza virus
AUTHOR(S): Plaue, S.
CORPORATE SOURCE: Neosyst. S.A., Strasbourg, 67100, Fr.
SOURCE: International Journal of Peptide & Protein Research (1990), 35(6), 510-17
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to mimic a well-known loop structure (site A) of the hemagglutinin of influenza virus, a series of cyclic peptides derived from the region 139-147 were synthesized. The lactam analogs cyclized between the N-terminus Cys 139 and the .beta.-carboxyl of aspartic acid 148 (small loop) or the .epsilon.-NH2 of lysine 148 via succinimidyl linker (large loop) were synthesized by the solid phase method. Cyclization was directly performed on the solid support prior to final cleavage of the peptide. Two protection schemes are reported which permit the obtaining of different loop sizes derived from the same sequence. Eight of the analogs contained relatively large ring structures (up to 38 membered). For the protection of the side chain of aspartic acid in combination with N-.alpha.-Fmoc protection, the cyclohexyl ester was more satisfactory than the benzyl ester with respect to imide formation. When the rate of cyclodimerization, as a function of resin substitution, was compared to the rate of cyclic monomer formation, it was found that dimerization was proportional to the concn. of the resin. Furthermore, a comparison of the recently reported BOP reagent over the classical DIPC/HOBt method for the cyclization reaction shows that in this case the reaction proceeded more rapidly by the BOP procedure although it gave a less pure product.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 15, 63

IT **130332-38-6DP**, polymer-bound 130332-41-1DP, polymer-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

IT **130332-36-4DP**, polymer-bound

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deprotection of)

IT **130332-38-6DP**, polymer-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 130332-38-6 HCAPLUS

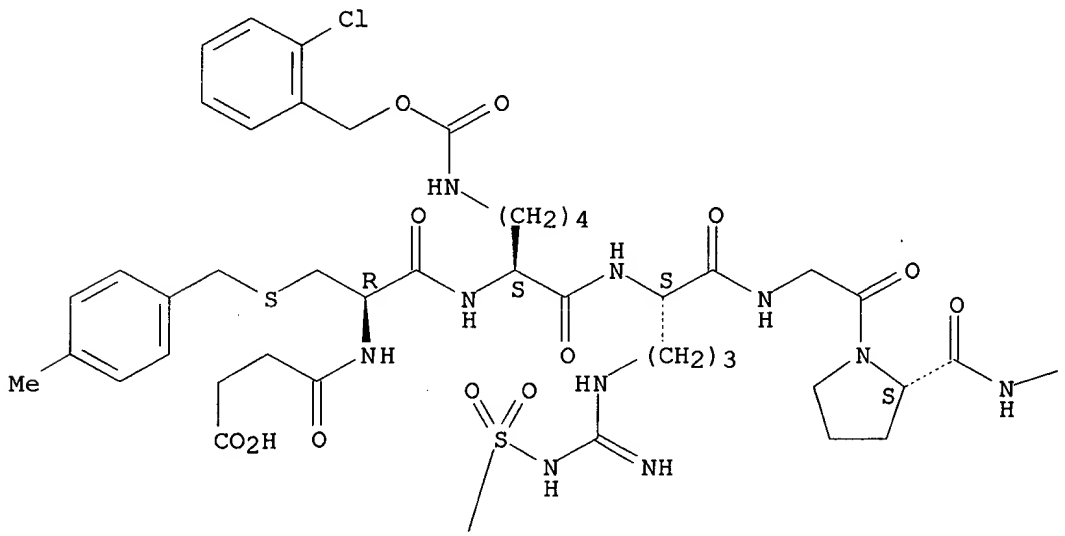
CN L-Tyrosinamide, N-(3-carboxy-1-oxopropyl)-S-[(4-methylphenyl)methyl]-L-cysteinyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl-L-prolylglycyl-O-(phenylmethyl)-L-seryl-L-.alpha.-aspartyl-L-phenylalanyl-L-lysyl-N-[bis(4-methylphenyl)methyl]-O-[(2,6-dichlorophenyl)methyl]-, 8-cyclohexyl ester, compd. with piperidine (1:1) (9CI) (CA INDEX NAME)

CM 1

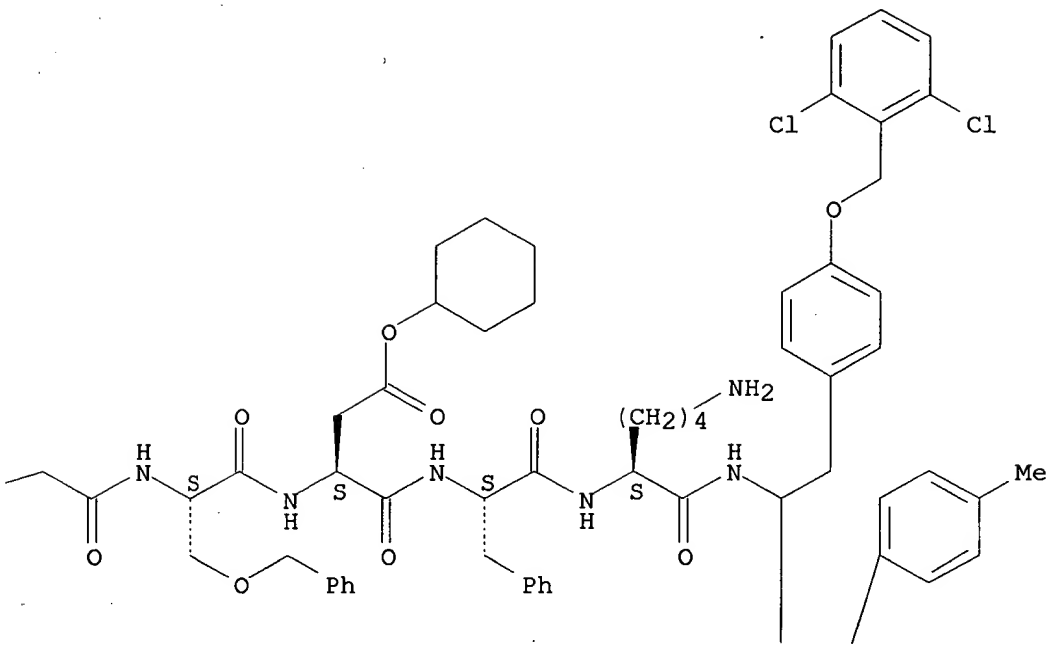
CRN 130332-37-5
CMF C117 H141 Cl3 N16 O22 S2

Absolute stereochemistry.

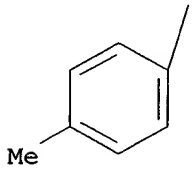
PAGE 1-A



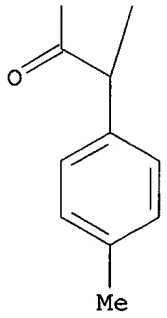
PAGE 1-B



PAGE 2-A



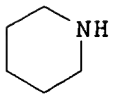
PAGE 2-B



CM 2

CRN 110-89-4

CMF C5 H11 N



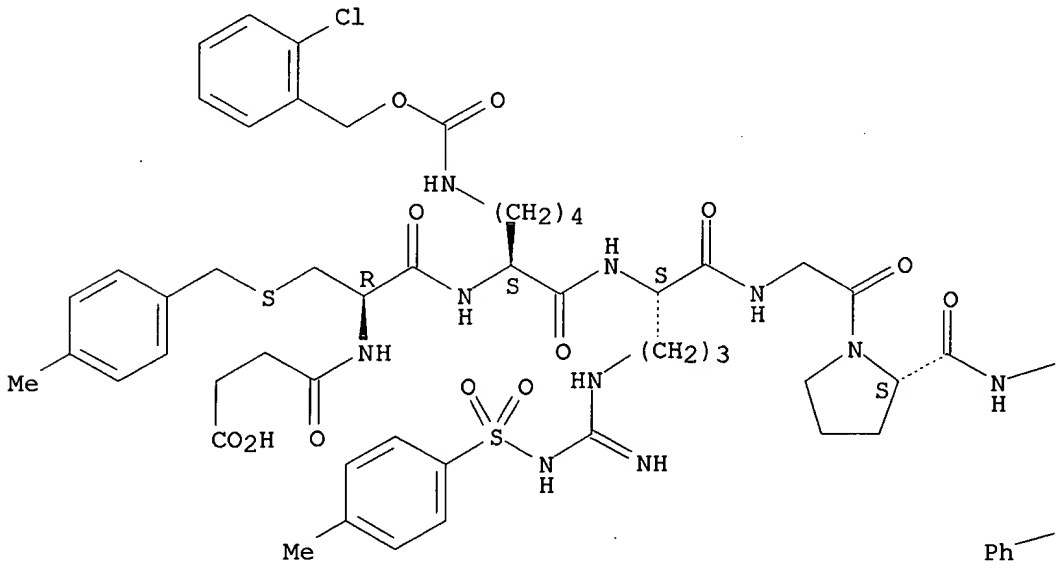
IT **130332-36-4DP**, polymer-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deprotection of)
RN 130332-36-4 HCAPLUS
CN L-Tyrosinamide, N-(3-carboxy-1-oxopropyl)-S-[(4-methylphenyl)methyl]-L-cysteinyl-N6-[[(2-chlorophenyl)methoxy]carbonyl]-L-lysyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl-L-prolylglycyl-O-(phenylmethyl)-L-seryl-L-.alpha.-aspartyl-L-phenylalanyl-N6-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-N-[bis(4-methylphenyl)methyl]-O-[(2,6-dichlorophenyl)methyl]-, 8-cyclohexyl ester, compd. with N-ethyl-N-(1-methylethyl)-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

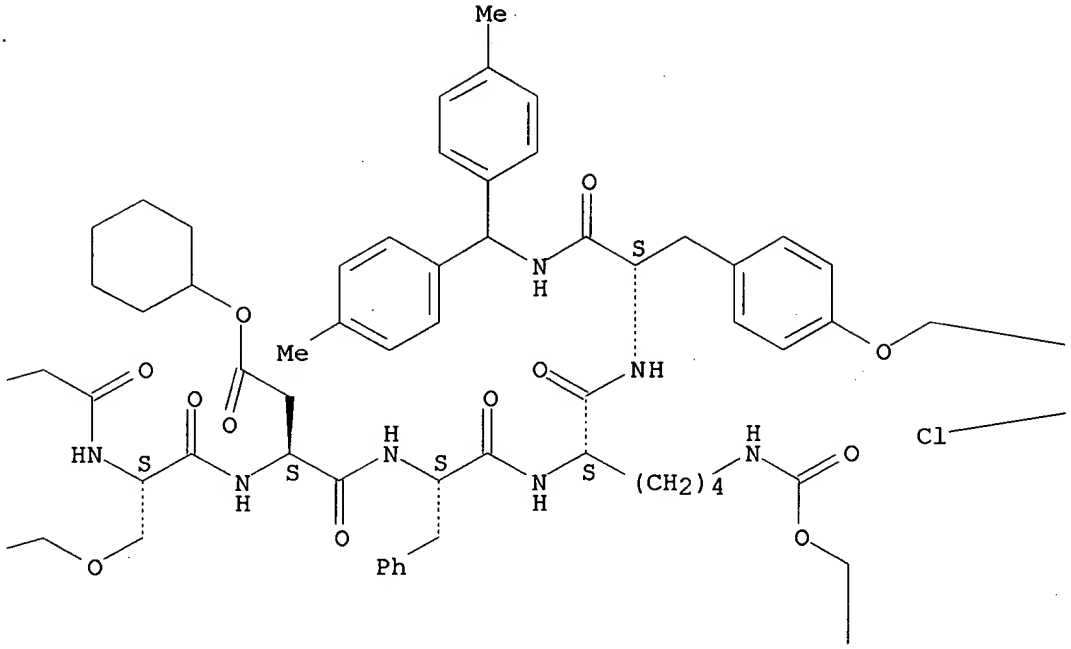
CRN 130332-35-3
CMF C132 H152 Cl3 N17 O24 S2

Absolute stereochemistry.

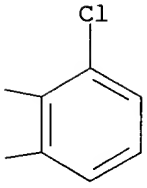
PAGE 1-A



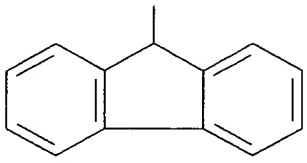
PAGE 1-B



PAGE 1-C

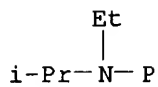


PAGE 2-B



CM 2

CRN 7087-68-5
CMF C8 H19 N



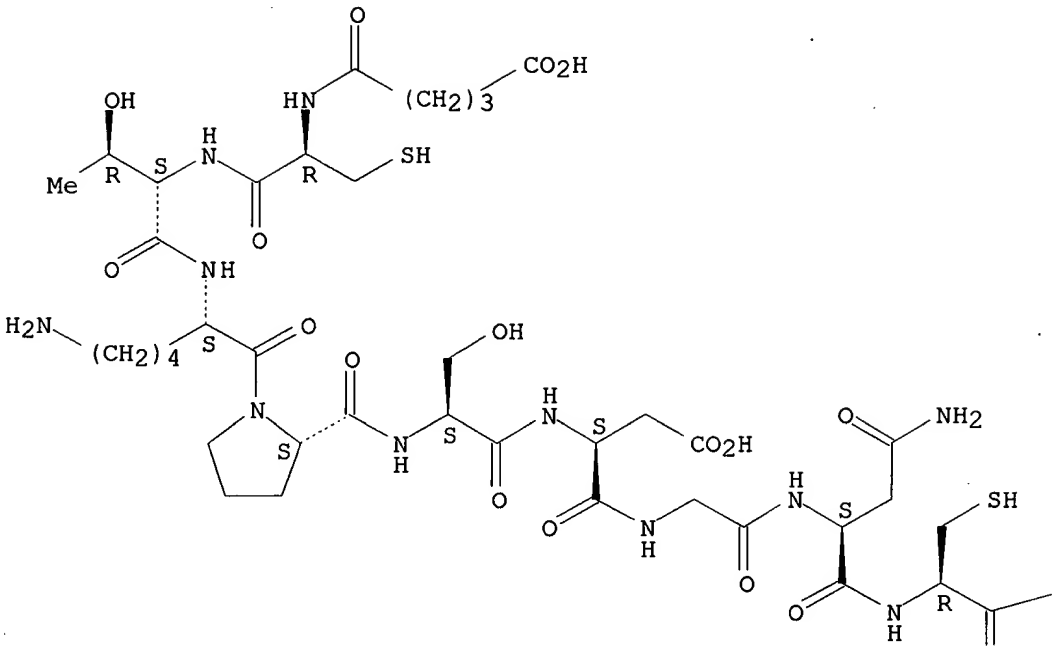
L9 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:551071 HCAPLUS
DOCUMENT NUMBER: 105:151071
TITLE: Immune response to synthetic peptide analogs of hepatitis B surface antigen and the binding assays between anti-peptide antisera and native HBsAg
AUTHOR(S): Zheng, Jian; Chen, Zhenzhen; Huang, Weiteh
CORPORATE SOURCE: Shanghai Inst. Biochem., Acad. Sin., Shanghai, Peop. Rep. China
SOURCE: Shengwu Huaxue Zazhi (1986), 2(3), 45-52
CODEN: SHZAE4; ISSN: 1000-8543
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Free or carrier-linked immunogens were prepd. from 3 synthetic peptides corresponding to the sequence of hepatitis B surface antigen (HBsAg). These immunogens were injected into rabbits, and most of them elicited an antipeptide response. Antisera against P122-148(ayw) and P122-148(adw) subtypes reacted with native HBsAg as shown by the Australia antibody test, in which the anti-P122-148(adw) sera showed higher reactivity than any other antipeptide antibodies ever reported. Structural anal. indicated that immunogens contg. the immunodominant regions of native proteins would be ideal candidates for the prepn. of efficient vaccines by synthetic methods.

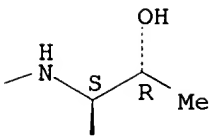
CC 15-2 (Immunochemistry)
IT **104413-40-3D**, bovine serum albumin conjugates 104413-41-4 104413-42-5
RL: BIOL (Biological study)
(antibodies to hepatitis B surface antigen induction by)
IT 25104-18-1DP, reaction products with succinyl peptides 38000-06-5DP, reaction products with succinyl peptides **104484-92-6DP**, reaction products with polylysine
RL: PREP (Preparation)
(prepn. of and antibodies to hepatitis B surface antigen induction by)
IT **104413-40-3D**, bovine serum albumin conjugates
RL: BIOL (Biological study)
(antibodies to hepatitis B surface antigen induction by)
RN 104413-40-3 HCAPLUS
CN L-Threonine, N-[N-[N2-[N-[N-[N-[1-[N2-[N-[N-(4-carboxy-1-oxobutyl)-L-cysteinyl]-L-threonyl]-L-lysyl]-L-prolyl]-L-seryl]-L-.alpha.-aspartyl]glycyl]-L-asparaginyl]-L-cysteinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-A

PAGE 2-B

IT **104484-92-6DP**, reaction products with polylysine
RL: PREP (Preparation)
(prepn. of and antibodies to hepatitis B surface antigen induction by)
RN 104484-92-6 HCAPLUS
CN L-Threonine, N-[N-[N2-[N-[N-[N-[1-[N2-[N-[N-(3-carboxy-1-oxopropyl)-L-cysteinyl]-L-threonyl]-L-lysyl]-L-prolyl]-L-seryl]-L-.alpha.-aspartyl]glycyl]-L-asparaginyl]-L-cysteinyl]- (9CI) (CA INDEX NAME)